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| (21) International Application Number: PCT/CA97/00829 (22) International Filing Date: 4 November 1997 (04.11.97) (30) Priority Data: 08/743,637 4 November 1996 (04.11.96) US (71) Applicant (for all designated States except US): INFECTIO DIAGNOSTIC (I.D.I.) INC. [CA/CA]; 4ème étage, 2050, boulevard René Lévesque Ouest, Sainte-Foy, Québec G1V 2K8 (CA). (72) Inventors; and (75) Inventors/Applicants (for US only): BERGERON, Michel, G. [CA/CA]; 2069, rue Brûlard, Sillery, Québec G1T 1G2 (CA). PICARD, François, J. [CA/CA]; 1245, rue de la Sapinière, Cap-Rouge, Québec G1Y 1A1 (CA). OUELLETTE, Marc [CA/CA]; 1035 de Ploermel, Sillery, Québec G1S 3S1 (CA). ROY, Paul, H. [US/US]; 28, rue Charles Garnier, Loretteville, Québec G2A 2X8 (CA). (74) Agents: DUBUC, Jean, H. et al.; Goudreau Gage Dubuc & Martineau Walker, The Stock Exchange Tower, Suite 3400, 800 Place Victoria, P.O. Box 242, Montreal, Québec H4Z 1E9 (CA). | | (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 13 August 1998 (13.08.98) |
| (54) Title: SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTIBIOTIC RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN MICROBIOLOGY LABORATORIES (57) Abstract DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample DNA from (i) any bacterium, (ii) the species <i>Streptococcus agalactiae</i> , <i>Staphylococcus saprophyticus</i> , <i>Enterococcus faecium</i> , <i>Neisseria meningitidis</i> , <i>Listeria monocytogenes</i> and <i>Candida albicans</i> , and (iii) any species of the genera <i>Streptococcus</i> , <i>Staphylococcus</i> , <i>Enterococcus</i> , <i>Neisseria</i> and <i>Candida</i> are disclosed. DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample antibiotic resistance genes selected from the group consisting of <i>bla_{tem}</i> , <i>bla_{rob}</i> , <i>bla_{shv}</i> , <i>bla_{oxa}</i> , <i>bla_Z</i> , <i>aadB</i> , <i>aacC1</i> , <i>aacC2</i> , <i>aacC3</i> , <i>aacA4</i> , <i>aacC6'-IIa</i> , <i>ermA</i> , <i>ermB</i> , <i>ermC</i> , <i>mecA</i> , <i>vanA</i> , <i>vanB</i> , <i>vanC</i> , <i>satA</i> , <i>aac(6'-aph(2''))</i> , <i>aad(6')</i> , <i>vat</i> , <i>vga</i> , <i>msrA</i> , <i>sul</i> and <i>int</i> are also disclosed. The above microbial species, genera and resistance genes are all clinically relevant and commonly encountered in a variety of clinical specimens. These DNA-based assays are rapid, accurate and can be used in clinical microbiology laboratories for routine diagnosis. These novel diagnostic tools should be useful to improve the speed and accuracy of diagnosis of microbial infections, thereby allowing more effective treatments. Diagnostic kits for (i) the universal detection and quantification of bacteria, and/or (ii) the detection, identification and quantification of the above-mentioned bacterial and fungal species and/or genera, and/or (iii) the detection, identification and quantification of the above-mentioned antibiotic resistance genes are also claimed. | | |

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TITLE OF THE INVENTION

**SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND
AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON
BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTIBIOTIC
5 RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN
MICROBIOLOGY LABORATORIES**

BACKGROUND OF THE INVENTION**Classical methods for the identification and susceptibility testing of bacteria**

10 Bacteria are classically identified by their ability to utilize different substrates as
a source of carbon and nitrogen through the use of biochemical tests such as the
API20E™ system (bioMérieux). For susceptibility testing, clinical microbiology
laboratories use methods including disk diffusion, agar dilution and broth microdilution.
Although identifications based on biochemical tests and antibacterial susceptibility
15 tests are cost-effective, at least two days are required to obtain preliminary results due
to the necessity of two successive overnight incubations to identify the bacteria from
clinical specimens as well as to determine their susceptibility to antimicrobial agents.
There are some commercially available automated systems (i.e. the MicroScan system
from Dade Diagnostics Corp. and the Vitek system from bioMérieux) which use
20 sophisticated and expensive apparatus for faster microbial identification and
susceptibility testing (Stager and Davis, 1992, Clin. Microbiol. Rev. 5:302-327). These
systems require shorter incubation periods, thereby allowing most bacterial
identifications and susceptibility testing to be performed in less than 6 hours.
Nevertheless, these faster systems always require the primary isolation of the bacteria
25 as a pure culture, a process which takes at least 18 hours for a pure culture or 2 days
for a mixed culture. The fastest identification system, the autoSCAN-Walk-Away™
system (Dade Diagnostics Corp.) identifies both gram-negative and gram-positive
bacterial species from standardized inoculum in as little as 2 hours and gives
susceptibility patterns to most antibiotics in 5.5 hours. However, this system has a
30 particularly high percentage (i.e. 3.3 to 40.5%) of non-conclusive identifications with
bacterial species other than *Enterobacteriaceae* (Croizé J., 1995, Lett. Infectiol.
10:109-113; York *et al.*, 1992, J. Clin. Microbiol. 30:2903-2910). For
Enterobacteriaceae, the percentage of non-conclusive identifications was 2.7 to 11.4%.

A wide variety of bacteria and fungi are routinely isolated and identified from
35 clinical specimens in microbiology laboratories. Tables 1 and 2 give the incidence for
the most commonly isolated bacterial and fungal pathogens from various types of
clinical specimens. These pathogens are the most frequently associated with
nosocomial and community-acquired human infections and are therefore considered
the most clinically important.

Clinical specimens tested in clinical microbiology laboratories

Most clinical specimens received in clinical microbiology laboratories are urine and blood samples. At the microbiology laboratory of the Centre Hospitalier de l'Université Laval (CHUL), urine and blood account for approximately 55% and 30% of the specimens received, respectively (Table 3). The remaining 15% of clinical specimens comprise various biological fluids including sputum, pus, cerebrospinal fluid, synovial fluid, and others (Table 3). Infections of the urinary tract, the respiratory tract and the bloodstream are usually of bacterial etiology and require antimicrobial therapy. In fact, all clinical samples received in the clinical microbiology laboratory are tested routinely for the identification of bacteria and susceptibility testing.

Conventional pathogen identification from clinical specimens**Urine specimens**

The search for pathogens in urine specimens is so preponderant in the routine microbiology laboratory that a myriad of tests have been developed. However, the gold standard remains the classical semi-quantitative plate culture method in which 1 µL of urine is streaked on plates and incubated for 18-24 hours. Colonies are then counted to determine the total number of colony forming units (CFU) per liter of urine. A bacterial urinary tract infection (UTI) is normally associated with a bacterial count of 10^7 CFU/L or more in urine. However, infections with less than 10^7 CFU/L in urine are possible, particularly in patients with a high incidence of diseases or those catheterized (Stark and Maki, 1984, N. Engl. J. Med. 311:560-564). Importantly, approximately 80% of urine specimens tested in clinical microbiology laboratories are considered negative (i.e. bacterial count of less than 10^7 CFU/L; Table 3). Urine specimens found positive by culture are further characterized using standard biochemical tests to identify the bacterial pathogen and are also tested for susceptibility to antibiotics. The biochemical and susceptibility testing normally require 18-24 hours of incubation.

Accurate and rapid urine screening methods for bacterial pathogens would allow a faster identification of negative specimens and a more efficient treatment and care management of patients. Several rapid identification methods (Uriscreen™, UTIscreen™, Flash Track™ DNA probes and others) have been compared to slower standard biochemical methods, which are based on culture of the bacterial pathogens. Although much faster, these rapid tests showed low sensitivities and poor specificities as well as a high number of false negative and false positive results (Koenig *et al.*, 1992, J. Clin. Microbiol. 30:342-345; Pezzlo *et al.*, 1992, J. Clin. Microbiol. 30:640-684).

Blood specimens

The blood specimens received in the microbiology laboratory are always submitted for culture. Blood culture systems may be manual, semi-automated or completely automated. The BACTEC system (from Becton Dickinson) and the

BacTAlert system (from Organon Teknika Corporation) are the two most widely used automated blood culture systems. These systems incubate blood culture bottles under optimal conditions for bacterial growth. Bacterial growth is monitored continuously to detect early positives by using highly sensitive bacterial growth detectors. Once growth is detected, a Gram stain is performed directly from the blood culture and then used to inoculate nutrient agar plates. Subsequently, bacterial identification and susceptibility testing are carried out from isolated bacterial colonies with automated systems as described previously. The bottles are normally reported as negative if no growth is detected after an incubation of 6 to 7 days. Normally, the vast majority of blood cultures are reported negative. For example, the percentage of negative blood cultures at the microbiology laboratory of the CHUL for the period February 1994-January 1995 was 93.1% (Table 3).

Other clinical samples

Upon receipt by the clinical microbiology laboratory, all body fluids other than blood and urine that are from normally sterile sites (i.e. cerebrospinal, synovial, pleural, pericardial and others) are processed for direct microscopic examination and subsequent culture. Again, most clinical samples are negative for culture (Table 3).

Regarding clinical specimens which are not from sterile sites such as sputum or stool specimens, the laboratory diagnosis by culture is more problematic because of the contamination by the normal flora. The bacterial pathogens potentially associated with the infection are purified from the contaminants and then identified as described previously. Of course, the universal detection of bacteria would not be useful for the diagnosis of bacterial infections at these non sterile sites. On the other hand, DNA-based assays for species or genus detection and identification as well as for the detection of antibiotic resistance genes from these specimens would be very useful and would offer several advantages over classical identification and susceptibility testing methods.

DNA-based assays with any clinical specimens

There is an obvious need for rapid and accurate diagnostic tests for bacterial detection and identification directly from clinical specimens. DNA-based technologies are rapid and accurate and offer a great potential to improve the diagnosis of infectious diseases (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). The DNA probes and amplification primers which are objects of the present invention are applicable for bacterial or fungal detection and identification directly from any clinical specimens such as blood cultures, blood, urine, sputum, cerebrospinal fluid, pus and other type of specimens (Table 3). The DNA-based tests proposed in this invention are superior in terms of both rapidity and accuracy to standard biochemical methods currently used for routine diagnosis from any clinical specimens in microbiology laboratories. Since

these tests are performed in around only one hour, they provide the clinicians with new diagnostic tools which should contribute to increase the efficiency of therapies with antimicrobial agents. Clinical specimens from organisms other than humans (e.g. other primates, birds, plants, mammals, farm animals, livestock and others) may also be tested with these assays.

A high percentage of culture negative specimens

Among all the clinical specimens received for routine diagnosis, approximately 80% of urine specimens and even more (around 95%) for other types of clinical specimens are negative for the presence of bacterial pathogens (Table 3). It would also be desirable, in addition to identify bacteria at the species or genus level in a given specimen, to screen out the high proportion of negative clinical specimens with a test detecting the presence of any bacterium (i.e. universal bacterial detection). Such a screening test may be based on the DNA amplification by PCR of a highly conserved genetic target found in all bacteria. Specimens negative for bacteria would not be amplified by this assay. On the other hand, those that are positive for bacteria would give a positive amplification signal with this assay.

Towards the development of rapid DNA-based diagnostic tests

A rapid diagnostic test should have a significant impact on the management of infections. DNA probe and DNA amplification technologies offer several advantages over conventional methods for the identification of pathogens and antibiotic resistance genes from clinical samples (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.; Ehrlich and Greenberg, 1994, PCR-based Diagnostics in Infectious Disease, Blackwell Scientific Publications, Boston, MA). There is no need for culture of the bacterial pathogens, hence the organisms can be detected directly from clinical samples, thereby reducing the time associated with the isolation and identification of pathogens. Furthermore, DNA-based assays are more accurate for bacterial identification than currently used phenotypic identification systems which are based on biochemical tests. Commercially available DNA-based technologies are currently used in clinical microbiology laboratories, mainly for the detection and identification of fastidious bacterial pathogens such as *Mycobacterium tuberculosis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* as well as for the detection of a variety of viruses (Podzorski and Persing, Molecular detection and identification of microorganisms, In : P. Murray *et al.*, 1995, Manual of Clinical Microbiology, ASM press, Washington D.C.). There are also other commercially available DNA-based assays which are used for culture confirmation assays.

Others have developed DNA-based tests for the detection and identification of bacterial pathogens which are objects of the present invention: *Staphylococcus* spp. (US patent application serial No. US 5 437 978), *Neisseria* spp. (US patent application

serial No. US 5 162 199 and European patent application serial No. EP 0 337 896 131) and *Listeria monocytogenes* (US patent applications serial Nos US 5 389 513 and US 5 089 386). However, the diagnostic tests described in these patents are based either on rRNA genes or on genetic targets different from those described in the present invention.

Although there are diagnostic kits or methods already used in clinical microbiology laboratories, there is still a need for an advantageous alternative to the conventional culture identification methods in order to improve the accuracy and the speed of the diagnosis of commonly encountered bacterial infections. Besides being much faster, DNA-based diagnostic tests are more accurate than standard biochemical tests presently used for diagnosis because the bacterial genotype (e.g. DNA level) is more stable than the bacterial phenotype (e.g. metabolic level).

Knowledge of the genomic sequences of bacterial and fungal species continuously increases as testified by the number of sequences available from databases. From the sequences readily available from databases, there is no indication therefrom as to their potential for diagnostic purposes. For determining good candidates for diagnostic purposes, one could select sequences for DNA-based assays for (i) the species-specific detection and identification of commonly encountered bacterial or fungal pathogens, (ii) the genus-specific detection and identification of commonly encountered bacterial or fungal pathogens, (iii) the universal detection of bacterial or fungal pathogens and/or (iv) the specific detection and identification of antibiotic resistance genes. All of the above types of DNA-based assays may be performed directly from any type of clinical specimens or from a microbial culture.

In our co-pending U.S. (N.S. 08/526,840) and PCT (PCT/CA/95/00528) patent applications, we described DNA sequences suitable for (i) the species-specific detection and identification of 12 clinically important bacterial pathogens, (ii) the universal detection of bacteria, and (iii) the detection of 17 antibiotic resistance genes. This co-pending application described proprietary DNA sequences and DNA sequences selected from databases (in both cases, fragments of at least 100 base pairs), as well as oligonucleotide probes and amplification primers derived from these sequences. All the nucleic acid sequences described in this patent application enter the composition of diagnostic kits and methods capable of a) detecting the presence of bacteria, b) detecting specifically the presence of 12 bacterial species and 17 antibiotic resistance genes. However, these methods and kits need to be improved, since the ideal kit and method should be capable of diagnosing close to 100% of microbial pathogens and antibiotic resistance genes. For example, infections caused by *Enterococcus faecium* have become a clinical problem because of its resistance to many antibiotics. Both the detection of these bacteria and the evaluation of their

resistance profiles are desirable. Besides that, novel DNA sequences (probes and primers) capable of recognizing the same and other microbial pathogens or the same and additional antibiotic resistance genes are also desirable to aim at detecting more target genes and complement our earlier patent application.

5

STATEMENT OF THE INVENTION

It is an object of the present invention to provide a specific, ubiquitous and sensitive method using probes and/or amplification primers for determining the presence and/or amount of nucleic acids:

10 - from specific microbial species or genera selected from the group consisting of *Streptococcus* species, *Streptococcus agalactiae*, *Staphylococcus* species, *Staphylococcus saprophyticus*, *Enterococcus* species, *Enterococcus faecium*, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes*, *Candida* species and *Candida albicans*

15 - from an antibiotic resistance gene selected from the group consisting of *bla_{tem}*, *bla_{rob}*, *bla_{shv}*, *bla_{oxa}*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *satA*, *aac(6')-aph(2'')*, *aad(6')*, *vat*, *vga*, *msrA*, *sul* and *int*, and optionally,

 - from any bacterial species

20 in any sample suspected of containing said nucleic acids,
 wherein each of said nucleic acids or a variant or part thereof comprises a selected target region hybridizable with said probe or primers;

 said method comprising the steps of contacting said sample with said probes or primers and detecting the presence and/or amount of hybridized probes or amplified
25 products as an indication of the presence and/or amount of said any bacterial species, specific microbial species or genus and antibiotic resistance gene.

 In a specific embodiment, a similar method directed to each specific microbial species or genus detection and identification, antibiotic resistance genes detection, and universal bacterial detection, separately, is provided.

30 In a more specific embodiment, the method makes use of DNA fragments (proprietary fragments and fragments obtained from databases), selected for their capacity to sensitively, specifically and ubiquitously detect the targeted bacterial or fungal nucleic acids.

 In a particularly preferred embodiment, oligonucleotides of at least 12
35 nucleotides in length have been derived from the longer DNA fragments, and are used in the present method as probes or amplification primers.

 The proprietary oligonucleotides (probes and primers) are also another object of the invention.

 Diagnostic kits comprising probes or amplification primers for the detection of

a microbial species or genus selected from the group consisting of *Streptococcus* species, *Streptococcus agalactiae*, *Staphylococcus* species, *Staphylococcus saprophyticus*, *Enterococcus* species, *Enterococcus faecium*, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes*, *Candida* species and *Candida albicans* are also objects of the present invention.

Diagnostic kits further comprising probes or amplification primers for the detection of an antibiotic resistance gene selected from the group consisting of *bla_{tem}*, *bla_{rob}*, *bla_{shv}*, *bla_{oxa}*, *bla_Z*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *satA*, *aac(6')-aph(2'')*, *aad(6')*, *vat*, *vga*, *msrA*, *sul* and *int* are also objects of this invention.

Diagnostic kits further comprising probes or amplification primers for the detection of any bacterial or fungal species, comprising or not comprising those for the detection of the specific microbial species or genus listed above, and further comprising or not comprising probes and primers for the antibiotic resistance genes listed above, are also objects of this invention.

In a preferred embodiment, such a kit allows for the separate or the simultaneous detection and identification of the above-listed microbial species or genus, antibiotic resistance genes and for the detection of any bacterium.

In the above methods and kits, amplification reactions may include a) polymerase chain reaction (PCR), b) ligase chain reaction, c) nucleic acid sequence-based amplification, d) self-sustained sequence replication, e) strand displacement amplification, f) branched DNA signal amplification, g) transcription-mediated amplification, h) cycling probe technology (CPT) i) nested PCR, or j) multiplex PCR.

In a preferred embodiment, a PCR protocol is used as an amplification reaction.

In a particularly preferred embodiment, a PCR protocol is provided, comprising, for each amplification cycle, an annealing step of 30 seconds at 45-55°C and a denaturation step of only one second at 95°C, without any time allowed specifically for the elongation step. This PCR protocol has been standardized to be suitable for PCR reactions with all selected primer pairs, which greatly facilitates the testing because each clinical sample can be tested with universal, species-specific, genus-specific and antibiotic resistance gene PCR primers under uniform cycling conditions. Furthermore, various combinations of primer pairs may be used in multiplex PCR assays.

We aim at developing a rapid test or kit to discard rapidly all the samples which are negative for bacterial cells and to subsequently detect and identify the above bacterial and/or fungal species and genera and to determine rapidly the bacterial resistance to antibiotics. Although the sequences from the selected antibiotic resistance genes are available from databases and have been used to develop DNA-based tests for their detection, our approach is unique because it represents a major improvement over current gold standard diagnostic methods based on bacterial

cultures. Using an amplification method for the simultaneous bacterial detection and identification and antibiotic resistance genes detection, there is no need for culturing the clinical sample prior to testing. Moreover, a modified PCR protocol has been developed to detect all target DNA sequences in approximately one hour under
5 uniform amplification conditions. This procedure will save lives by optimizing treatment, will diminish antibiotic resistance because less antibiotics will be prescribed, will reduce the use of broad spectrum antibiotics which are expensive, decrease overall health care costs by preventing or shortening hospitalizations, and decrease the time and costs associated with clinical laboratory testing.

10 In the methods and kits described herein below, the oligonucleotide probes and amplification primers have been derived from larger sequences (i.e. DNA fragments of at least 100 base pairs). All DNA fragments have been obtained either from proprietary fragments or from databases. DNA fragments selected from databases are newly used in a method of detection according to the present invention, since they
15 have been selected for their diagnostic potential.

It is clear to the individual skilled in the art that other oligonucleotide sequences appropriate for (i) the universal bacterial detection, (ii) the detection and identification of the above microbial species or genus and (iii) the detection of antibiotic resistance genes other than those listed in Annex VI may also be derived from the proprietary
20 fragments or selected database sequences. For example, the oligonucleotide primers or probes may be shorter or longer than the ones we have chosen; they may also be selected anywhere else in the proprietary DNA fragments or in the sequences selected from databases; they may be also variants of the same oligonucleotide. If the target DNA or a variant thereof hybridizes to a given oligonucleotide, or if the target DNA or
25 a variant thereof can be amplified by a given oligonucleotide PCR primer pair, the converse is also true; a given target DNA may hybridize to a variant oligonucleotide probe or be amplified by a variant oligonucleotide PCR primer. Alternatively, the oligonucleotides may be designed from any DNA fragment sequences for use in amplification methods other than PCR. Consequently, the core of this invention is the
30 identification of universal, species-specific, genus-specific and resistance gene-specific genomic or non-genomic DNA fragments which are used as a source of specific and ubiquitous oligonucleotide probes and/or amplification primers. Although the selection and evaluation of oligonucleotides suitable for diagnostic purposes requires much effort, it is quite possible for the individual skilled in the art to derive, from the selected
35 DNA fragments, oligonucleotides other than the ones listed in Annex VI which are suitable for diagnostic purposes. When a proprietary fragment or a database sequence is selected for its specificity and ubiquity, it increases the probability that subsets thereof will also be specific and ubiquitous.

Since a high percentage of clinical specimens are negative for bacteria (Table

3), DNA fragments having a high potential for the selection of universal oligonucleotide probes or primers were selected from proprietary and database sequences. The amplification primers were selected from a gene highly conserved in bacteria and fungi, and are used to detect the presence of any bacterial pathogen in clinical specimens in order to determine rapidly (approximately one hour) whether it is positive or negative for bacteria. The selected gene, designated *tuf*, encodes a protein (EF-Tu) involved in the translational process during protein synthesis. The *tuf* gene sequence alignments used to derive the universal primers include both proprietary and database sequences (Example 1 and Annex I). This strategy allows the rapid screening of the numerous negative clinical specimens (around 80% of the specimens received, see Table 3) submitted for bacteriological testing. Tables 4, 5 and 6 provide a list of the bacterial or fungal species used to test the specificity of PCR primers and DNA probes. Table 7 gives a brief description of each species-specific, genus-specific and universal amplification assays which are objects of the present invention. Tables 8, 9 and 10 provide some relevant information about the proprietary and database sequences selected for diagnostic purposes.

DETAILED DESCRIPTION OF THE INVENTION

Development of species-specific, genus-specific, universal and antibiotic resistance gene-specific DNA probes and amplification primers for microorganisms

Selection from databases of sequences suitable for diagnostic purposes

In order to select sequences which are suitable for species-specific or genus-specific detection and identification of bacteria or fungi or, alternatively, for the universal detection of bacteria, the database sequences (GenBank, EMBL and Swiss-Prot) were chosen based on their potential for diagnostic purposes according to sequence information and computer analysis performed with these sequences. Initially, all sequence data available for the targeted microbial species or genus were carefully analyzed. The gene sequences which appeared the most promising for diagnostic purposes based on sequence information and on sequence comparisons with the corresponding gene in other microbial species or genera performed with the Genetics Computer Group (GCG, Wisconsin) programs were selected for testing by PCR. Optimal PCR amplification primers were chosen from the selected database sequences with the help of the Oligo™ 4.0 primer analysis software (National Biosciences Inc., Plymouth, Minn.). The chosen primers were tested in PCR assays for their specificity and ubiquity for the target microbial species or genus. In general, the identification of database sequences from which amplification primers suitable for species-specific or genus-specific detection and identification were selected involved the computer analysis and PCR testing of several candidate gene sequences before

obtaining a primer pair which is specific and ubiquitous for the target microbial species or genus. Annex VI provides a list of selected specific and ubiquitous PCR primer pairs. Annexes I to V and Examples 1 to 4 illustrate the strategy used to select genus-specific, species-specific and universal PCR primers from *tuf* sequences or from the *recA* gene.

Oligonucleotide primers and probes design and synthesis

The DNA fragments sequenced by us or selected from databases (GenBank and EMBL) were used as sources of oligonucleotides for diagnostic purposes. For this strategy, an array of suitable oligonucleotide primers or probes derived from a variety of genomic DNA fragments (size of more than 100 bp) selected from databases were tested for their specificity and ubiquity in PCR and hybridization assays as described later. It is important to note that the database sequences were selected based on their potential for being species-specific, genus-specific or universal for the detection of bacteria or fungi according to available sequence information and extensive analysis and that, in general, several candidate database sequences had to be tested in order to obtain the desired specificity, ubiquity and sensitivity.

Oligonucleotide probes and amplification primers derived from species-specific fragments selected from database sequences were synthesized using an automated DNA synthesizer (Perkin-Elmer Corp., Applied Biosystems Division). Prior to synthesis, all oligonucleotides (probes for hybridization and primers for DNA amplification) were evaluated for their suitability for hybridization or DNA amplification by polymerase chain reaction (PCR) by computer analysis using standard programs (i.e. the Genetics Computer Group (GCG) programs and the primer analysis software Oligo™ 4.0). The potential suitability of the PCR primer pairs was also evaluated prior to the synthesis by verifying the absence of unwanted features such as long stretches of one nucleotide and a high proportion of G or C residues at the 3' end (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.).

The oligonucleotide primers or probes may be derived from either strand of the duplex DNA. The primers or probes may consist of the bases A, G, C, or T or analogs and they may be degenerated at one or more chosen nucleotide position(s). The primers or probes may be of any suitable length and may be selected anywhere within the DNA sequences from proprietary fragments or from selected database sequences which are suitable for (i) the universal detection of bacteria, (ii) the species-specific detection and identification of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae* and *Candida albicans* (iii) the genus-specific detection of *Streptococcus* species, *Enterococcus* species, *Staphylococcus* species and *Neisseria* species or (iv) the detection of the 26 above-mentioned clinically important antibiotic resistance genes.

Variants for a given target bacterial gene are naturally occurring and are attributable to sequence variation within that gene during evolution (Watson *et al.*, 1987, Molecular Biology of the Gene, 4th ed., The Benjamin/Cummings Publishing Company, Menlo Park, CA; Lewin, 1989, Genes IV, John Wiley & Sons, New York, NY). For example, different strains of the same bacterial species may have a single or more nucleotide variation(s) at the oligonucleotide hybridization site. The person skilled in the art is well aware of the existence of variant bacterial or fungal DNA sequences for a specific gene and that the frequency of sequence variations depends on the selective pressure during evolution on a given gene product. The detection of a variant sequence for a region between two PCR primers may be demonstrated by sequencing the amplification product. In order to show the presence of sequence variants at the primer hybridization site, one has to amplify a larger DNA target with PCR primers outside that hybridization site. Sequencing of this larger fragment will allow the detection of sequence variation at this site. A similar strategy may be applied to show variants at the hybridization site of a probe. Insofar as the divergence of the target sequences or a part thereof does not affect the specificity and ubiquity of the amplification primers or probes, variant bacterial DNA is under the scope of this invention. Variants of the selected primers or probes may also be used to amplify or hybridize to a variant DNA.

20 **Sequencing of *tuf* sequences from a variety of bacterial and fungal species**

The nucleotide sequence of a portion of *tuf* genes was determined for a variety of bacterial and fungal species. The amplification primers SEQ ID NOs: 107 and 108, which amplify a *tuf* gene portion of approximately 890 bp, were used for the sequencing of bacterial *tuf* sequences. The amplification primers SEQ ID NOs: 109 and 172, which amplify a *tuf* gene portion of approximately 830 bp, were used for the sequencing of fungal *tuf* sequences. Both primer pairs can amplify *tufA* and *tufB* genes. This is not surprising because these two genes are nearly identical. For example, the entire *tufA* and *tufB* genes from *E. coli* differ at only 13 nucleotide positions (Neidhardt *et al.*, 1996, *Escherichia coli* and *Salmonella*: Cellular and Molecular Biology, 2nd ed., American Society for Microbiology Press, Washington, D.C.). These amplification primers are degenerated at several nucleotide positions and contain inosines in order to allow the amplification of a wide range of *tuf* sequences. The strategy used to select these amplification primers is similar to that illustrated in Annex I for the selection of universal primers. The amplification primers SEQ ID NOs: 107 and 108 could be used to amplify the *tuf* genes from any bacterial species. The amplification primers SEQ ID NOs: 109 and 172 could be used to amplify the *tuf* genes from any fungal species.

The *tuf* genes were amplified directly from bacterial or yeast cultures using the following amplification protocol: One μ L of cell suspension was transferred directly to

19 μ L of a PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl₂, 1 μ M of each of the 2 primers, 200 μ M of each of the four dNTPs, 0.5 unit of *Taq* DNA polymerase (Promega Corp., Madison, WI). PCR reactions were subjected to cycling using a MJ Research PTC-200 thermal cycler (MJ Research Inc., Watertown, Mass.) as follows: 3 min at 96°C followed by 30-35 cycles of 1 min at 95°C for the denaturation step, 1 min at 30-50°C for the annealing step and 1 min at 72°C for the extension step. Subsequently, twenty microliters of the PCR-amplified mixture were resolved by electrophoresis in a 1.5% agarose gel. The gel was then visualized by staining with methylene blue (Flores *et al.*, 1992, Biotechniques, 13:203-205). The size of the amplification products was estimated by comparison with a 100-bp molecular weight ladder. The band corresponding to the specific amplification product (i.e. approximately 890 or 830 bp for bacterial or fungal *tuf* sequences, respectively) was excised from the agarose gel and purified using the QIAquick™ gel extraction kit (QIAGEN Inc., Chatsworth, CA). The gel-purified DNA fragment was then used directly in the sequencing protocol. Both strands of the *tuf* genes amplification product were sequenced by the dideoxynucleotide chain termination sequencing method by using an Applied Biosystems automated DNA sequencer (model 373A) with their PRISM™ Sequenase® Terminator Double-stranded DNA Sequencing Kit (Perkin-Elmer Corp., Applied Biosystems Division, Foster City, CA). The sequencing reactions were all performed by using the amplification primers (SEQ ID NOs: 107 to 109 and 172) and 100 ng per reaction of the gel-purified amplicon. In order to ensure that the determined sequence did not contain errors attributable to the sequencing of PCR artefacts, we have sequenced two preparations of the gel-purified *tuf* amplification product originating from two independent PCR amplifications. For all target microbial species, the sequences determined for both amplicon preparations were identical. Furthermore, the sequences of both strands were 100% complementary thereby confirming the high accuracy of the determined sequence. The *tuf* sequences determined using the above strategy are all in the Sequence Listing (i.e. SEQ ID NOs:118 to 146). Table 13 gives the originating microbial species and the source for each *tuf* sequence in the Sequence Listing.

The alignment of the *tuf* sequences determined by us or selected from databases reveals clearly that the length of the sequenced portion of the *tuf* genes is variable. There may be insertions or deletions of several amino acids. This explains why the size of the sequenced *tuf* amplification product was variable for both bacterial and fungal species. Among the *tuf* sequences determined by our group, we found insertions and deletions adding up to 5 amino acids or 15 nucleotides. Consequently, the nucleotide positions indicated on top of each of Annexes I to V do not correspond for *tuf* sequences having insertions or deletions.

It should also be noted that the various *tuf* sequences determined by us

occasionally contain degenerescences. These degenerated nucleotides correspond to sequence variations between *tufA* and *tufB* genes because the amplification primers amplify both *tuf* genes. These nucleotide variations were not attributable to nucleotide misincorporations by the *taq* DNA polymerase because the sequence of both strands were identical and also because the sequences determined with both preparations of the gel-purified *tuf* amplicons were identical.

The selection of amplification primers from *tuf* sequences

The *tuf* sequences determined by us or selected from databases were used to select PCR primers for (i) the universal detection of bacteria, (ii) the genus-specific detection and identification of *Enterococcus* spp. and *Staphylococcus* spp. and (iii) the species-specific detection and identification of *Candida albicans*. The strategy used to select these PCR primers was based on the analysis of multiple sequence alignments of various *tuf* sequences. For more details about the selection of PCR primers from *tuf* sequences, please refer to Examples 1 to 3 and Annexes I to IV.

The selection of amplification primers from *recA*

The comparison of the nucleotide sequence for the *recA* gene from various bacterial species including 5 species of streptococci allowed the selection of *Streptococcus*-specific PCR primers. For more details about the selection of PCR primers from *recA*, please refer to Example 4 and Annex V.

DNA fragment isolation from *Staphylococcus saprophyticus* by arbitrarily primed PCR

DNA sequences of unknown coding potential for the species-specific detection and identification of *Staphylococcus saprophyticus* were obtained by the method of arbitrarily primed PCR (AP-PCR).

AP-PCR is a method which can be used to generate specific DNA probes for microorganisms (Fani *et al.*, 1993, Mol. Ecol. 2:243-250). A description of the AP-PCR protocol used to isolate a species-specific genomic DNA fragment from *Staphylococcus saprophyticus* follows. Twenty different oligonucleotide primers of 10 nucleotides in length (all included in the AP-PCR kit OPAD (Operon Technologies, Inc., Alameda, CA)) were tested systematically with DNAs from 3 bacterial strains of *Staphylococcus saprophyticus* (all obtained from the American Type Culture Collection (ATCC): numbers 15305, 35552 and 43867) as well as with DNA from four other staphylococcal species (*Staphylococcus aureus* ATCC 25923, *Staphylococcus epidermidis* ATCC 14990, *Staphylococcus haemolyticus* ATCC 29970 and *Staphylococcus hominis* ATCC 35982). For all bacterial species, amplification was performed from a bacterial suspension adjusted to a standard 0.5 McFarland which corresponds to approximately 1.5×10^8 bacteria/mL. One μL of the standardized bacterial suspension was transferred directly to 19 μL of a PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl_2 ,

1.2 μ M of only one of the 20 different AP-PCR primers OPAD, 200 μ M of each of the four dNTPs and 0.5 unit of *Taq* DNA polymerase (Promega Corp., Madison, WI). PCR reactions were subjected to cycling using a MJ Research PTC-200 thermal cycler (MJ Research Inc.) as follows: 3 min at 96°C followed by 35 cycles of 1 min at 95°C for the denaturation step, 1 min at 32°C for the annealing step and 1 min at 72°C for the extension step. A final extension step of 7 min at 72°C was made after the 35 cycles to ensure complete extension of PCR products. Subsequently, twenty microliters of the PCR amplified mixture were resolved by electrophoresis in a 2% agarose gel containing 0.25 μ g/mL of ethidium bromide. The size of the amplification products was estimated by comparison with a 50-bp molecular weight ladder.

Amplification patterns specific for *Staphylococcus saprophyticus* were observed with the AP-PCR primer OPAD-9 (SEQ ID NO: 25). Amplification with this primer consistently showed a band corresponding to a DNA fragment of approximately 450 bp for all *Staphylococcus saprophyticus* strains tested but not for any of the four other staphylococcal species tested. This species-specific pattern was confirmed by testing 10 more clinical isolates of *S. saprophyticus* selected from the culture collection of the microbiology laboratory of the CHUL as well as strains selected from the gram-positive bacterial species listed in Table 5.

The band corresponding to the approximately 450 bp amplicon which was specific and ubiquitous for *S. saprophyticus* based on AP-PCR was excised from the agarose gel and purified using the QIAquick™ gel extraction kit (QIAGEN Inc.). The gel-purified DNA fragment was cloned into the T/A cloning site of the pCR 2.1™ plasmid vector (Invitrogen Inc.) using T4 DNA ligase (New England BioLabs). Recombinant plasmids were transformed into *E. coli* DH5 α competent cells using standard procedures. Plasmid DNA isolation was done by the method of Birnboim and Doly (Nucleic Acids Res. 7:1513-1523) for small-scale preparations. All plasmid DNA preparations were digested with the *Eco*RI restriction endonuclease to ensure the presence of the approximately 450 bp AP-PCR insert into the recombinant plasmids. Subsequently, a large-scale and highly purified plasmid DNA preparation was performed from two selected clones shown to carry the AP-PCR insert by using the QIAGEN plasmid purification kit. These plasmid preparations were used for automated DNA sequencing.

Both strands of the AP-PCR insert from the two selected clones were sequenced by the dideoxynucleotide chain termination sequencing method with SP6 and T7 sequencing primers, by using an Applied Biosystems automated DNA sequencer as described previously. The analysis of the obtained sequences revealed that the DNA sequences for both strands from each clone were 100% complementary. Furthermore, it showed that the entire sequence determined for each clone were both identical. These sequencing data confirm the 100% accuracy for the determined 438

bp sequence (SEQ ID NO: 29). Optimal amplification primers have been selected from the sequenced AP-PCR *Staphylococcus saprophyticus* DNA fragment with the help of the primer analysis software Oligo™ 4.0. The selected primer sequences have been tested in PCR assays to verify their specificity and ubiquity (Table 7). These PCR
5 primers were specific since there was no amplification with DNA from bacterial species other than *S. saprophyticus* selected from Tables 4 and 5. Furthermore, this assay was ubiquitous since 245 of 260 strains of *S. saprophyticus* were efficiently amplified with this PCR assay. When used in combination with another *S. saprophyticus*-specific PCR assay, which is an object of our co-pending U.S. (N.S. 08/526,840) and PCT
10 (PCT/CA95/00528) patent applications, the ubiquity reaches 100% for these 260 strains.

DNA amplification

For DNA amplification by the widely used PCR (polymerase chain reaction) method, primer pairs were derived from proprietary DNA fragments or from database
15 sequences. Prior to synthesis, the potential primer pairs were analyzed by using the Oligo™ 4.0 software to verify that they are good candidates for PCR amplification.

During DNA amplification by PCR, two oligonucleotide primers binding respectively to each strand of the heat-denatured target DNA from the bacterial genome are used to amplify exponentially *in vitro* the target DNA by successive
20 thermal cycles allowing denaturation of the DNA, annealing of the primers and synthesis of new targets at each cycle (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.).

Briefly, the PCR protocols were as follow: Treated clinical specimens or
25 standardized bacterial or fungal suspensions (see below) were amplified in a 20 µL PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 2.5 mM MgCl₂, 0.4 µM of each primer, 200 µM of each of the four dNTPs and 0.5 unit of *Taq* DNA polymerase (Promega) combined with the TaqStart™ antibody (Clontech Laboratories Inc., Palo Alto, CA). The TaqStart™ antibody, which is a neutralizing monoclonal
30 antibody to *Taq* DNA polymerase, was added to all PCR reactions to enhance the specificity and the sensitivity of the amplifications (Kellogg *et al.*, 1994, Biotechniques 16:1134-1137). The treatment of the clinical specimens varies with the type of specimen tested, since the composition and the sensitivity level required are different for each specimen type. It consists in a rapid protocol to lyse the bacterial cells and
35 eliminate the PCR inhibitory effects (see example 11 for urine specimen preparation). For amplification from bacterial or fungal cultures, the samples were added directly to the PCR amplification mixture without any pre-treatment step (see example 10). Primer sequences derived from highly conserved regions of the bacterial 16S ribosomal RNA gene were used to provide an internal control for all PCR reactions. Alternatively, the

internal control was derived from sequences not found in microorganisms or in the human genome. The internal control was integrated into all amplification reactions to verify the efficiency of the PCR assays and to ensure that significant PCR inhibition was absent. The internal control derived from rRNA was also useful to monitor the efficiency of bacterial lysis protocols.

PCR reactions were then subjected to thermal cycling (3 min at 95°C followed by 30 cycles of 1 second at 95°C for the denaturation step and 30 second at 55°C for the annealing-extension step) using a PTC-200 thermal cycler (MJ Research Inc.) and subsequently analyzed by standard ethidium bromide-stained agarose gel electrophoresis. The number of cycles performed for the PCR assays varies according to the sensitivity level required. For example, the sensitivity level required for microbial detection directly from clinical specimens is higher for blood specimens than for urine specimens because the concentration of microorganisms associated with a septicemia can be much lower than that associated with a urinary tract infection. Consequently, more sensitive PCR assays having more thermal cycles are required for direct detection from blood specimens. Similarly, PCR assays performed directly from bacterial or fungal cultures may be less sensitive than PCR assays performed directly from clinical specimens because the number of target organisms is normally much lower in clinical specimens than in microbial cultures.

It is clear that other methods for the detection of specific amplification products, which may be faster and more practical for routine diagnosis, may be used. Such methods may be based on the detection of fluorescence after amplification (e.g. TaqMan™ system from Perkin Elmer or Amplisensor™ from Biotronics). Methods based on the detection of fluorescence are particularly promising for utilization in routine diagnosis as they are very rapid, quantitative and can be automated (Example 14).

Microbial pathogens detection and identification may also be performed by solid support or liquid hybridization using species-specific internal DNA probes hybridizing to an amplification product. Such probes may be generated from any species-specific or genus-specific DNA amplification products which are objects of the present invention. Alternatively, the internal probes for species or genus detection and identification may be derived from the amplicons produced by the universal amplification assay. The oligonucleotide probes may be labeled with biotin or with digoxigenin or with any other reporter molecules.

To assure PCR efficiency, glycerol, dimethyl sulfoxide (DMSO) or other related solvents can be used to increase the sensitivity of the PCR and to overcome problems associated with the amplification of a target DNA having a high GC content or forming strong secondary structures (Dieffenbach and Dveksler, 1995, PCR Primer : A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, New York). The

concentration ranges for glycerol and DMSO are 5-15% (v/v) and 3-10% (v/v), respectively. For the PCR reaction mixture, the concentration ranges for the amplification primers and MgCl_2 are 0.1-1.5 μM and 1.5-3.5 mM, respectively. Modifications of the standard PCR protocol using external and nested primers (i.e. nested PCR) or using more than one primer pair (i.e. multiplex PCR) may also be used (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). For more details about the PCR protocols and amplicon detection methods, see Examples 9 to 14.

The person skilled in the art of DNA amplification knows the existence of other rapid amplification procedures such as ligase chain reaction (LCR), transcription-mediated amplification (TMA), self-sustained sequence replication (3SR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA), branched DNA (bDNA) and cycling probe technology (CPT) (Lee *et al.*, 1997, Nucleic Acid Amplification Technologies: Application to Disease Diagnosis, Eaton Publishing, Boston, MA ; Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). The scope of this invention is not limited to the use of amplification by PCR, but rather includes the use of any rapid nucleic acid amplification method or any other procedure which may be used to increase rapidity and sensitivity of the tests. Any oligonucleotide suitable for the amplification of nucleic acids by approaches other than PCR and derived from the species-specific, genus-specific and universal DNA fragments as well as from selected antibiotic resistance gene sequences included in this document are also under the scope of this invention.

Hybridization assays with oligonucleotide probes

In hybridization experiments, single-stranded oligonucleotides (size less than 100 nucleotides) have some advantages over DNA fragment probes for the detection of bacteria, such as ease of synthesis in large quantities, consistency in results from batch to batch and chemical stability. Briefly, for the hybridizations, oligonucleotides were 5' end-labeled with the radionucleotide $\gamma\text{-}^{32}\text{P(dATP)}$ using T4 polynucleotide kinase (Pharmacia) (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). The unincorporated radionucleotide was removed by passing the labeled oligonucleotide through a Sephadex G-50TM column. Alternatively, oligonucleotides were labeled with biotin, either enzymatically at their 3' ends or incorporated directly during synthesis at their 5' ends, or with digoxigenin. It will be appreciated by the person skilled in the art that labeling means other than the three above labels may be used.

Each oligonucleotide probe was then tested for its specificity by hybridization to DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6. All of the bacterial or fungal species tested were likely to be pathogens associated

with common infections or potential contaminants which can be isolated from clinical specimens. Each target DNA was released from bacterial cells using standard chemical treatments to lyse the cells (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Subsequently, the DNA was denatured by conventional methods and then irreversibly fixed onto a solid support (e.g. nylon or nitrocellulose membranes) or free in solution. The fixed single-stranded target DNAs were then hybridized with the oligonucleotide probe cells (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Pre-hybridization conditions were in 1 M NaCl + 10% dextran sulfate + 1% SDS + 100 µg/mL salmon sperm DNA at 65°C for 15 min. Hybridization was performed in fresh pre-hybridization solution containing the labeled probe at 65°C overnight. Post-hybridization washing conditions were as follows: twice in 3X SSC containing 1% SDS, twice in 2X SSC containing 1% SDS and twice in 1X SSC containing 1% SDS (all of these washes were at 65°C for 15 min), and a final wash in 0.1X SSC containing 1% SDS at 25°C for 15 min. Autoradiography of washed filters allowed the detection of selectively hybridized probes. Hybridization of the probe to a specific target DNA indicated a high degree of similarity between the nucleotide sequence of these two DNAs because of the high stringency of the washes.

An oligonucleotide probe was considered specific only when it hybridized solely to DNA from the species or genus from which it was isolated. Oligonucleotide probes found to be specific were subsequently tested for their ubiquity (i.e. ubiquitous probes recognized most or all isolates of the target species or genus) by hybridization to microbial DNAs from clinical isolates of the species or genus of interest including ATCC strains. The DNAs from strains of the target species or genus were denatured, fixed onto nylon membranes and hybridized as described above. Probes were considered ubiquitous when they hybridized specifically with the DNA from at least 80% of the isolates of the target species or genus.

Specificity and ubiquity tests for oligonucleotide primers and probes

The specificity of oligonucleotide primers and probes, derived either from the DNA fragments sequenced by us or selected from databases, was tested by amplification of DNA or by hybridization with bacterial or fungal species selected from those listed in Tables 4, 5 and 6, as described in the two previous sections. Oligonucleotides found to be specific were subsequently tested for their ubiquity by amplification (for primers) or by hybridization (for probes) with bacterial DNAs from isolates of the target species or genus. Results for specificity and ubiquity tests with the oligonucleotide primers are summarized in Table 7. The specificity and ubiquity of the PCR assays using the selected amplification primer pairs were tested directly from cultures (see Examples 9 and 10) of bacterial or fungal species.

The various species-specific and genus-specific PCR assays which are objects of the present invention are all specific. For the PCR assays specific to bacterial species or genus, this means that DNA isolated from a wide variety of bacterial species, other than that from the target species or genus and selected from Tables 4 and 5, could not be amplified. For the PCR assay specific to *Candida albicans*, it means there was no amplification with genomic DNA from the fungal species listed in Table 6 as well as with a variety of bacterial species selected from Tables 4 and 5.

The various species-specific and genus-specific PCR assays which are objects of the present invention are also all ubiquitous (Table 7). (i) The species-specific PCR assays for *E. faecium*, *L. monocytogenes*, *S. saprophyticus*, *S. agalactiae* and *C. albicans* amplified genomic DNA from all or most strains of the target species tested, which were obtained from various sources and which are representative of the diversity within each target species (Table 7). The species identification of all of these strains was based on classical biochemical methods which are routinely used in clinical microbiology laboratories. (ii) The genus-specific PCR assays specific for *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp. and *Neisseria* spp. amplified genomic DNA from all or most strains of the target genus tested, which represent all clinically important bacterial species for each target genus. These strains were obtained from various sources and are representative of the diversity within each target genus. Again, the species identification of all of these strains was based on classical biochemical methods which are routinely used in clinical microbiology laboratories. More specifically, the four genus-specific PCR assays amplified the following species: (1) The *Enterococcus*-specific assay amplified efficiently DNA from all of the 11 enterococcal species tested including *E. avium*, *E. casseliflavus*, *E. dispar*, *E. durans*, *E. faecalis*, *E. faecium*, *E. flavescens*, *E. gallinarum*, *E. hirae*, *E. mundtii* and *E. raffinosus*. (2) The *Neisseria*-specific assay amplified efficiently DNA from all of the 12 neisserial species tested including *N. canis*, *N. cinerea*, *N. elongata*, *N. flavescens*, *N. gonorrhoeae*, *N. lactamica*, *N. meningitidis*, *N. mucosa*, *N. polysaccharea*, *N. sicca*, *N. subflava* and *N. weaveri*. (3) The *Staphylococcus*-specific assay amplified efficiently DNA from 13 of the 14 staphylococcal species tested including *S. aureus*, *S. auricularis*, *S. capitis*, *S. cohnii*, *S. epidermidis*, *S. haemolyticus*, *S. hominis*, *S. lugdunensis*, *S. saprophyticus*, *S. schleiferi*, *S. simulans*, *S. warneri* and *S. xylosus*. The staphylococcal species which could not be amplified is *S. sciuri*. (4) Finally, the *Streptococcus*-specific assay amplified efficiently DNA from all of the 22 streptococcal species tested including *S. agalactiae*, *S. anginosus*, *S. bovis*, *S. constellatus*, *S. crista*, *S. dysgalactiae*, *S. equi*, *S. gordonii*, *S. intermedius*, *S. mitis*, *S. mutans*, *S. oralis*, *S. parasanguis*, *S. pneumoniae*, *S. pyogenes*, *S. salivarius*, *S. sanguis*, *S. sabrinus*, *S. suis*, *S. uberis*, *S. vestibularis* and *S. viridans*. On the other hand, the *Streptococcus*-specific assay did not amplify 3 out of 9 strains

of *S. mutans* and 1 out of 23 strains of *S. salivarius*, thereby showing a slight lack of ubiquity for these two streptococcal species.

All specific and ubiquitous amplification primers for each target microbial species or genus or antibiotic resistance gene investigated are listed in Annex VI.

5 Divergence in the sequenced DNA fragments can occur, insofar as the divergence of these sequences or a part thereof does not affect the specificity of the probes or amplification primers. Variant bacterial DNA is under the scope of this invention.

The PCR amplification primers listed in Annex VI were all tested for their specificity and ubiquity using reference strains as well as clinical isolates from various
10 geographical locations. The 351 reference strains used to test the amplification and hybridization assays (Tables 4, 5 and 6) were obtained from (i) the American Type Culture Collection (ATCC): 85%, (ii) the Laboratoire de santé publique du Québec (LSPQ): 10%, (iii) the Centers for Disease Control and Prevention (CDC): 3% , (iv) the National Culture Type Collection (NCTC): 1% and (v) several other reference
15 laboratories throughout the world: 1%. These reference strains are representative of (i) 90 gram-negative bacterial species (169 strains; Table 4), (ii) 97 gram-positive bacterial species (154 strains; Table 5) and (iii) 12 fungal species (28 strains; Table 6).

Antibiotic resistance genes

Antimicrobial resistance complicates treatment and often leads to therapeutic
20 failures. Furthermore, overuse of antibiotics inevitably leads to the emergence of bacterial resistance. Our goal is to provide clinicians, in approximately one hour, the needed information to prescribe optimal treatments. Besides the rapid identification of negative clinical specimens with DNA-based tests for universal bacterial detection and the identification of the presence of a specific pathogen in the positive specimens with
25 species- and/or genus-specific DNA-based tests, clinicians also need timely information about the ability of the bacterial pathogen to resist antibiotic treatments. We feel that the most efficient strategy to evaluate rapidly bacterial resistance to antimicrobials is to detect directly from the clinical specimens the most common and clinically important antibiotic resistance genes (i.e. DNA-based tests for the detection
30 of antibiotic resistance genes). Since the sequence from the most important and common bacterial antibiotic resistance genes are available from databases, our strategy was to use the sequence from a portion or from the entire resistance gene to design specific oligonucleotide primers or probes which will be used as a basis for the development of rapid DNA-based tests. The sequence from each of the bacterial
35 antibiotic resistance genes selected on the basis of their clinical relevance (i.e. high incidence and importance) is given in the Sequence Listing. Tables 9 and 10 summarize some characteristics of the selected antibiotic resistance genes. Our approach is unique because the antibiotic resistance genes detection and the bacterial detection and identification are performed simultaneously in multiplex assays under

uniform PCR amplification conditions (Example 13).

Annex VI provides a list of all amplification primers selected from 26 clinically important antibiotic resistance genes which were tested in PCR assays. The various PCR assays for antibiotic resistance genes detection and identification were validated by testing several resistant bacterial isolates known to carry the targeted gene and obtained from various countries. The testing of a large number of strains which do not carry the targeted resistance gene was also performed to ensure that all assays were specific. So far, all PCR assays for antibiotic resistance genes are highly specific and have detected all control resistant bacterial strains known to carry the targeted gene. The results of some clinical studies to validate the array of PCR assays for the detection and identification of antibiotic resistance genes and correlate these DNA-based assays with standard antimicrobials susceptibility testing methods are presented in Tables 11 and 12.

Universal bacterial detection

In the routine microbiology laboratory, a high percentage of clinical specimens sent for bacterial identification are negative by culture (Table 4). Testing clinical samples with universal amplification primers or universal probes to detect the presence of bacteria prior to specific identification and screen out the numerous negative specimens is thus useful as it saves costs and may rapidly orient the clinical management of the patients. Several amplification primers and probes were therefore synthesized from highly conserved portions of bacterial sequences from the *tuf* genes (Table 8). The universal primer selection was based on a multiple sequence alignment constructed with sequences determined by us or selected from available database sequences as described in Example 1 and Annex I.

For the identification of database sequences suitable for the universal detection of bacteria, we took advantage of the fact that the complete genome sequences for two distant microorganisms (i.e. *Mycoplasma genitalium* and *Haemophilus influenzae*) are available. A comparison of the amino acid sequence for all proteins encoded by the genome of these two distant microorganisms led to the identification of highly homologous proteins. An analysis of these homologous proteins allowed to select some promising candidates for the development of universal DNA-based assays for the detection of bacteria. Since the complete nucleotide sequence of several other microbial genomes are presently available in databases, a person skilled in the art could arrive to the same conclusions by comparing genomes sequences other than those of *Mycoplasma genitalium* and *Haemophilus influenzae*. The selected *tuf* gene encodes a protein (EF-Tu) involved in the translation process during protein synthesis. Subsequently, an extensive nucleotide sequence analysis was performed with the *tuf* gene sequences available in databases as well as with novel *tuf* sequences which we have determined as described previously. All computer analysis of amino acid and

nucleotide sequences were performed by using the GCG programs. Subsequently, optimal PCR primers for the universal amplification of bacteria were selected with the help of the Oligo™ program. The selected primers are degenerated at several nucleotide positions and contain several inosines in order to allow the amplification of all clinically relevant bacterial species (Annex I). Inosine is a nucleotide analog able to specifically bind to any of the four nucleotides A, C, G or T. Degenerated oligonucleotides consist of an oligonucleotide mix having two or more of the four nucleotides A, C, G or T at the site of mismatches. The inclusion of inosine and/or of degenerescences in the amplification primers allow mismatch tolerance thereby permitting the amplification of a wider array of target nucleotide sequences (Dieffenbach and Dveksler, 1995 PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, NY).

The amplification conditions with the universal primers were identical to those used for the species- and genus-specific amplification assays except that the annealing temperature was 50°C instead of 55°C. This universal PCR assay was specific and nearly ubiquitous for the detection of bacteria. The specificity for bacteria was verified by amplifying genomic DNA isolated from the 12 fungal species listed in Table 6 as well as genomic DNA from *Leishmania donovani*, *Saccharomyces cerevisiae* and human lymphocytes. None of the above eukaryotic DNA preparations could be amplified by the universal assay, thereby suggesting that this test is specific for bacteria. The ubiquity of the universal assay was verified by amplifying genomic DNAs from 116 reference strains which represent 95 of the most clinically relevant bacterial species. These species have been selected from the bacterial species listed in Tables 4 and 5. We found that 104 of these 116 strains could be amplified. The bacterial species which could not be amplified belong to the following genera: *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species). Sequencing of the *tuf* genes from these bacterial species has been recently performed. This sequencing data has been used to select new universal primers which may be more ubiquitous. These primers are in the process of being tested. We also observed that for several species the annealing temperature had to be reduced to 45°C in order to get an efficient amplification. These bacterial species include *Gemella morbilbrum*, *Listeria* spp. (3 species) and *Gardnerella vaginalis*. It is important to note that the 95 bacterial species selected from Tables 4 and 5 to test the ubiquity of the universal assay include all of the most clinically relevant bacterial species associated with a variety of human infections acquired in the community or in hospitals (nosocomial infections). The most clinically important bacterial and fungal pathogens are listed in Tables 1 and 2.

EXAMPLES AND ANNEXES

The following examples and annexes are intended to be illustrative of the various methods and compounds of the invention, rather than limiting the scope thereof.

- 5 The various annexes show the strategies used for the selection of amplification primers from *tuf* sequences or from the *recA* gene: (i) Annex I illustrates the strategy used for the selection of the universal amplification primers from *tuf* sequences. (ii) Annex II shows the strategy used for the selection of the amplification primers specific for the genus *Enterococcus* from *tuf* sequences. (iii) Annex III illustrates the strategy
10 used for the selection of the amplification primers specific for the genus *Staphylococcus* from *tuf* sequences. (iv) Annex IV shows the strategy used for the selection of the amplification primers specific for the species *Candida albicans* from *tuf* sequences. (v) Annex V illustrates the strategy used for the selection of the amplification primers specific for the genus *Streptococcus* from *recA* sequences. (vi)
15 Annex VI gives a list of all selected primer pairs. As shown in these annexes, the selected amplification primers may contain inosines and/or degenerescences. Inosine is a nucleotide analog able to specifically bind to any of the four nucleotides A, C, G or T. Alternatively, degenerated oligonucleotides which consist of an oligonucleotide mix having two or more of the four nucleotides A, C, G or T at the site of mismatches
20 were used. The inclusion of inosine and/or of degenerescences in the amplification primers allow mismatch tolerance thereby permitting the amplification of a wider array of target nucleotide sequences (Dieffenbach and Dveksler, 1995 PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, New York).

EXAMPLES

25 EXAMPLE 1 :

- Selection of universal PCR primers from *tuf* sequences. As shown in Annex I, the comparison of *tuf* sequences from a variety of bacterial and eukaryotic species allowed the selection of PCR primers which are universal for the detection of bacteria. The strategy used to design the PCR primers was based on the analysis of a multiple
30 sequence alignment of various *tuf* sequences. This multiple sequence alignment includes *tuf* sequences from 38 bacterial species and 3 eukaryotic species either determined by us or selected from databases (Table 13). A careful analysis of this multiple sequence alignment allowed the selection of primer sequences which are conserved within eubacteria but which discriminate sequences from eukaryotes,
35 thereby permitting the universal detection of bacteria. As shown in Annex I, the selected primers contain several inosines and degenerescences. This was necessary because there is a relatively high polymorphism among bacterial *tuf* sequences despite the fact that this gene is highly conserved. In fact, among the *tuf* sequences that we determined, we found many nucleotide variations as well as some deletions and/or

insertions of amino acids. The selected universal primers were specific and ubiquitous for bacteria (Table 7). Of the 95 most clinically important bacterial species tested, 12 were not amplified. These species belong to the genera *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species). The universal primers did not amplify DNA of non-bacterial origin, including human and other types of eukaryotic DNA.

EXAMPLE 2 :

Selection of genus-specific PCR primers from *tuf* sequences. As shown in Annexes 2 and 3, the comparison of *tuf* sequences from a variety of bacterial species allowed the selection of PCR primers specific for *Enterococcus* spp. or for *Staphylococcus* spp. The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various *tuf* sequences. These multiple sequence alignments include the *tuf* sequences of four representative bacterial species selected from each target genus as well as *tuf* sequences from species of other closely related bacterial genera. A careful analysis of those alignments allowed the selection of oligonucleotide sequences which are conserved within the target genus but which discriminate sequences from other closely related genera, thereby permitting the genus-specific and ubiquitous detection and identification of the target bacterial genus.

For the selection of primers specific for *Enterococcus* spp. (Annex II), we have sequenced a portion of approximately 890 bp of the *tuf* genes for *Enterococcus avium*, *E. faecalis*, *E. faecium* and *E. gallinarum*. All other *tuf* sequences used in the alignment were either sequenced by us or selected from databases. The analysis of this sequence alignment led to the selection of a primer pair specific and ubiquitous for *Enterococcus* spp. (Table 7). All of the 11 enterococcal species tested were efficiently amplified and there was no amplification with genomic DNA from bacterial species of other genera.

For the selection of primers specific for *Staphylococcus* spp. (Annex III), we have also sequenced a portion of approximately 890 bp of the *tuf* genes for *Staphylococcus aureus*, *S. epidermidis*, *S. saprophyticus* and *S. simulans*. All other *tuf* sequences used in the alignment were either sequenced by us or selected from databases. The analysis of this sequence alignment led to the selection of two primer pairs specific and ubiquitous for *Staphylococcus* spp. (Table 7). Annex III shows the strategy used to select one of these two PCR primer pairs. The same strategy was used to select the other primer pair. Of the 14 staphylococcal species tested, one (*S. sciuri*) could not be amplified by the *Staphylococcus*-specific PCR assays using either one of these two primer pairs. For PCR assays using either one of these two primer pairs, there was no amplification with DNA from species of other bacterial genera.

EXAMPLE 3 :

Selection from *tuf* sequences of PCR primers specific for *Candida albicans*. As shown in Annex IV, the comparison of *tuf* sequences from a variety of bacterial and eukaryotic species allowed the selection of PCR primers specific for *Candida albicans*.

- 5 The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various *tuf* sequences. This multiple sequence alignment includes *tuf* sequences of five representative fungal species selected from the genus *Candida* which were determined by our group (i.e. *C. albicans*, *C. glabrata*, *C. krusei*, *C. parapsilosis* and *C. tropicalis*) as well as *tuf* sequences from other closely related
- 10 fungal species. *tuf* sequences from various bacterial species were also included. A careful analysis of this sequence alignment allowed the selection of primers from the *C. albicans* *tuf* sequence; these primers discriminate sequences from other closely related *Candida* species and other fungal species, thereby permitting the species-specific and ubiquitous detection and identification of *C. albicans* (Table 7). All of 88
- 15 *Candida albicans* strains tested were efficiently amplified and there was no amplification with genomic DNA from other fungal or bacterial species.

EXAMPLE 4:

Selection of PCR primers specific for *Streptococcus* from *recA*. As shown in Annex V, the comparison of the various bacterial *recA* gene sequences available from

20 databases (GenBank and EMBL) was used as a basis for the selection of PCR primers which are specific and ubiquitous for the bacterial genus *Streptococcus*. Since sequences of the *recA* gene are available for many bacterial species including five species of streptococci, it was possible to choose sequences well conserved within the genus *Streptococcus* but distinct from the *recA* sequences for other bacterial genera.

- 25 When there were mismatches between the *recA* gene sequences from the five *Streptococcus* species, an inosine residue was incorporated into the primer (Annex V). The selected primers, each containing one inosine and no degenerescence, were specific and ubiquitous for *Streptococcus* species (Table 7). This PCR assay amplified all of the 22 streptococcal species tested. However, the *Streptococcus*-specific assay
- 30 did not amplify DNA from 3 out of 9 strains of *S. mutans* and 1 out of 3 strains of *S. salivarius*. There was no amplification with genomic DNA from other bacterial genera (Table 7).

EXAMPLE 5:

Nucleotide sequencing of DNA fragments. The nucleotide sequence of a portion

35 of the *tuf* genes from a variety of bacterial or fungal species was determined by using the dideoxynucleotide chain termination sequencing method (Sanger *et al.*, 1977, Proc. Natl. Acad. Sci. USA. 74:5463-5467). The sequencing was performed by using an Applied Biosystems automated DNA sequencer (model 373A) with their PRISM™ Sequenase® Terminator Double-stranded DNA Sequencing Kit (Perkin-Elmer Corp.,

Applied Biosystems Division, Foster City, CA). The sequencing strategy does not discriminate *tufA* and *tufB* genes because the sequencing primers hybridize efficiently to both bacterial *tuf* genes. These DNA sequences are shown in the sequence listing (SEQ ID Nos: 118 to 146). The presence of several degenerated nucleotides in the various *tuf* sequences determined by our group (Table 13) corresponds to sequence variations between *tufA* and *tufB*.

Oligonucleotide primers and probes selection. Oligonucleotide probes and amplification primers were selected from the given proprietary DNA fragments or database sequences using the Oligo™ program and were synthesized with an automated ABI DNA synthesizer (Model 391, Perkin-Elmer Corp., Applied Biosystems Division) using phosphoramidite chemistry.

EXAMPLE 6 :

Labeling of oligonucleotides for hybridization assays. Each oligonucleotide was 5' end-labeled with γ -³²P (dATP) by the T4 polynucleotide kinase (Pharmacia) as described earlier. The label could also be non-radioactive.

Specificity test for oligonucleotide probes. All labeled oligonucleotide probes were tested for their specificity by hybridization to DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6 as described earlier. Species-specific or genus-specific probes were those hybridizing only to DNA from the microbial species or genus from which it was isolated. Oligonucleotide probes found to be specific were submitted to ubiquity tests as follows.

Ubiquity test for oligonucleotide probes. Specific oligonucleotide probes were then used in ubiquity tests with strains of the target species or genus including reference strains and other strains obtained from various countries and which are representative of the diversity within each target species or genus. Chromosomal DNAs from the isolates were transferred onto nylon membranes and hybridized with labeled oligonucleotide probes as described for specificity tests. The batteries of isolates constructed for each target species or genus contain reference ATCC strains as well as a variety of clinical isolates obtained from various sources. Ubiquitous probes were those hybridizing to at least 80% of DNAs from the battery of clinical isolates of the target species or genus.

EXAMPLE 7:

Same as example 6 except that a pool of specific oligonucleotide probes is used for microbial identification (i) to increase sensitivity and assure 100% ubiquity or (ii) to identify simultaneously more than one microbial species and/or genus. Microbial identification could be performed from microbial cultures or directly from any clinical specimen.

EXAMPLE 8:

Same as example 6 except that bacteria or fungi were detected directly from clinical samples. Any biological sample was loaded directly onto a dot blot apparatus and cells were lysed *in situ* for bacterial or fungal detection and identification. Blood samples should be heparinized in order to avoid coagulation interfering with their convenient loading on a dot blot apparatus.

EXAMPLE 9:

PCR amplification. The technique of PCR was used to increase the sensitivity and the rapidity of the assays. The sets of primers were tested in PCR assays performed directly from bacterial colonies or from a standardized bacterial suspension (see Example 10) to determine their specificity and ubiquity (Table 7). Examples of specific and ubiquitous PCR primer pairs are listed in Annex VI.

Specificity and ubiquity tests for amplification primers. The specificity of all selected PCR primer pairs was tested against DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6 as described earlier. Primer pairs found specific for each species or genus were then tested for their ubiquity to ensure that each set of primers could amplify at least 90% of DNAs from a battery of isolates of the target species or genus. The batteries of isolates constructed for each species contain reference ATCC strains and various clinical isolates from around the world which are representative of the diversity within each species or genus.

Standard precautions to avoid false positive PCR results should be taken (Kwok and Higuchi, 1989, Nature, 239:237-238). Methods to inactivate PCR amplification products such as the inactivation by uracil-N-glycosylase may be used to control PCR carryover.

EXAMPLE 10:

Amplification directly from bacterial or yeast cultures. PCR assays were performed either directly from a bacterial colony or from a bacterial suspension, the latter being adjusted to a standard McFarland 0.5 (corresponds to approximately 1.5×10^8 bacteria/mL). In the case of direct amplification from a colony, a portion of a colony was transferred using a plastic rod directly into a 20 μ L PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM $MgCl_2$, 0.4 μ M of each primer, 200 μ M of each of the four dNTPs and 0.5 unit of Taq DNA polymerase (Promega) combined with the TaqStart™ antibody (Clontech Laboratories Inc.). For the bacterial suspension, 1 μ L of the cell suspension was added to 19 μ L of the same PCR reaction mixture. For the identification from yeast cultures, 1 μ L of a standard McFarland 1.0 (corresponds to approximately 3.0×10^8 bacteria/mL) concentrated 100 times by centrifugation was added directly to the PCR reaction. This concentration step for yeast cells was performed because a McFarland 0.5 for yeast cells has approximately 200 times fewer cells than a McFarland 0.5 for bacterial cells.

PCR reactions were then subjected to thermal cycling (3 min at 95°C followed by 30 cycles of 1 second at 95°C for the denaturation step and 30 seconds at 55°C for the annealing-extension step) using a PTC-200 thermal cycler. PCR amplification products were then analyzed by standard agarose gel (2%) electrophoresis.

- 5 Amplification products were visualized in agarose gels containing 0.25 $\mu\text{g/mL}$ of ethidium bromide under UV at 254 nm. The entire PCR assay can be completed in approximately one hour.

Primer sequences derived from highly conserved regions of the bacterial 16S ribosomal RNA gene were used to provide an internal control for all PCR reactions.

- 10 Alternatively, the internal control was derived from sequences not found in microorganisms or in the human genome. The internal control was integrated into all amplification reactions to verify the efficiency of the PCR assays and to ensure that significant PCR inhibition was absent. The internal control derived from rRNA was also useful to monitor the efficiency of the bacterial lysis protocols. The internal control and
15 the species-specific or genus-specific amplifications were performed simultaneously in multiplex PCR assays.

EXAMPLE 11:

- Amplification directly from urine specimens. For PCR amplification performed directly from urine specimens, 1 μL of urine was mixed with 4 μL of a lysis solution
20 containing 500 mM KCl, 100 mM tris-HCl (pH 9.0), 1% triton X-100. After incubation for at least 15 minutes at room temperature, 1 μL of the treated urine specimen was added directly to 19 μL of the PCR reaction mixture. The final concentration of the PCR reagents was 50 mM KCl, 10 mM Tris (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl_2 , 0.4 μM of each primer, 200 μM of each of the four dNTPs. In addition, each
25 μL reaction contained 0.5 unit of *Taq* DNA polymerase (Promega) combined with the TaqStart™ antibody (Clontech Laboratories Inc.).

Strategies for the internal control, PCR amplification and agarose gel detection of the amplicons are as previously described in example 10.

EXAMPLE 12:

- 30 Detection of antibiotic resistance genes. The presence of specific antibiotic resistance genes which are frequently encountered and clinically relevant is identified using the PCR amplification or hybridization protocols described previously. Specific oligonucleotides used as a basis for the DNA-based tests are selected from the antibiotic resistance gene sequences. These tests, which allow the rapid evaluation of
35 bacterial resistance to antimicrobial agents, can be performed either directly from clinical specimens, from a standardized bacterial suspension or from a bacterial colony and should complement diagnostic tests for the universal detection of bacteria as well as for the species-specific and genus-specific microbial detection and identification.

EXAMPLE 13:

Same as examples 10 and 11 except that assays were performed by multiplex PCR (i.e. using several pairs of primers in a single PCR reaction) to reach an ubiquity of 100% for the specific targeted pathogen(s). For more heterogeneous microbial species or genus, a combination of PCR primer pairs may be required to detect and identify all representatives of the target species or genus.

Multiplex PCR assays could also be used to (i) detect simultaneously several microbial species and/or genera or, alternatively, (ii) to simultaneously detect and identify bacterial and/or fungal pathogens and detect specific antibiotic resistance genes either directly from a clinical specimen or from bacterial cultures.

For these applications, amplicon detection methods should be adapted to differentiate the various amplicons produced. Standard agarose gel electrophoresis could be used because it discriminates the amplicons based on their sizes. Another useful strategy for this purpose would be detection using a variety of fluorescent dyes emitting at different wavelengths. The fluorescent dyes can be each coupled with a specific oligonucleotide linked to a fluorescence quencher which is degraded during amplification to release the fluorescent dyes (e.g. TaqMan™, Perkin Elmer).

EXAMPLE 14:

Detection of amplification products. The person skilled in the art will appreciate that alternatives other than standard agarose gel electrophoresis (Example 10) may be used for the revelation of amplification products. Such methods may be based on fluorescence polarization or on the detection of fluorescence after amplification (e.g. Amplisensor™, Biotronics; TaqMan™, Perkin-Elmer Corp.) or other labels such as biotin (SHARP Signal™ system, Digene Diagnostics). These methods are quantitative and may be automated. One of the amplification primers or an internal oligonucleotide probe specific to the amplicon(s) derived from the species-specific, genus-specific or universal DNA fragments is coupled with the fluorescent dyes or with any other label. Methods based on the detection of fluorescence are particularly suitable for diagnostic tests since they are rapid and flexible as fluorescent dyes emitting at different wavelengths are available.

EXAMPLE 15:

Species-specific, genus-specific, universal and antibiotic resistance gene amplification primers can be used in other rapid amplification procedures such as the ligase chain reaction (LCR), transcription-mediated amplification (TMA), self-sustained sequence replication (3SR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA), cycling probe technology (CPT) and branched DNA (bDNA) or any other methods to increase the sensitivity of the test. Amplifications can be performed from isolated bacterial cultures or directly from any clinical specimen. The scope of this invention is therefore not limited to the use of the

DNA sequences from the enclosed Sequence Listing for PCR only but rather includes the use of any procedures to specifically detect bacterial DNA and which may be used to increase rapidity and sensitivity of the tests.

EXAMPLE 16:

5 A test kit would contain sets of probes specific for each microbial species or genus as well as a set of universal probes. The kit is provided in the form of test components, consisting of the set of universal probes labeled with non-radioactive labels as well as labeled species- or genus-specific probes for the detection of each pathogen of interest in specific types of clinical samples. The kit will also include test
10 reagents necessary to perform the pre-hybridization, hybridization, washing steps and hybrid detection. Finally, test components for the detection of known antibiotic resistance genes (or derivatives therefrom) will be included. Of course, the kit will include standard samples to be used as negative and positive controls for each hybridization test.

15 Components to be included in the kits will be adapted to each specimen type and to detect pathogens commonly encountered in that type of specimen. Reagents for the universal detection of bacteria will also be included. Based on the sites of infection, the following kits for the specific detection of pathogens may be developed:

20 - A kit for the universal detection of bacterial or fungal pathogens from all clinical specimens which contains sets of probes specific for highly conserved regions of the microbial genomes.

25 - A kit for the detection of microbial pathogens retrieved from urine samples, which contains 5 specific test components (sets of probes for the detection of *Enterococcus faecium*, *Enterococcus* species, *Staphylococcus saprophyticus*, *Staphylococcus* species and *Candida albicans*).

 - A kit for the detection of respiratory pathogens which contains 3 specific test components (sets of probes for the detection of *Staphylococcus* species, *Enterococcus* species and *Candida albicans*).

30 - A kit for the detection of pathogens retrieved from blood samples, which contains 10 specific test components (sets of probes for the detection of *Streptococcus* species, *Streptococcus agalactiae*, *Staphylococcus* species, *Staphylococcus saprophyticus*, *Enterococcus* species, *Enterococcus faecium*, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes* and *Candida albicans*). This kit can also be applied for direct detection and identification from blood
35 cultures.

 - A kit for the detection of pathogens causing meningitis, which contains 5 specific test components (sets of probes for the detection of *Streptococcus* species, *Listeria monocytogenes*, *Neisseria meningitidis*, *Neisseria* species and *Staphylococcus* species).

- A kit for the detection of clinically important antibiotic resistance genes which contains sets of probes for the specific detection of at least one of the 26 following genes associated with antibiotic resistance: *bla_{tem}*, *bla_{rob}*, *bla_{shv}*, *bla_{oxa}*, *bla_Z*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*,
 5 *satA*, *aac(6')-aph(2'')*, *aad(6')*, *vat*, *vga*, *msrA*, *sul* and *int*.

- Other kits adapted for the detection of pathogens from skin, abdominal wound or any other clinically relevant infections may also be developed.

EXAMPLE 17:

Same as example 16 except that the test kits contain all reagents and controls
 10 to perform DNA amplification assays. Diagnostic kits will be adapted for amplification by PCR (or other amplification methods) performed directly either from clinical specimens or from microbial cultures. Components required for (i) universal bacterial detection, (ii) species-specific and genus-specific bacterial and/or fungal detection and identification and (iii) detection of antibiotic resistance genes will be included.

15 Amplification assays could be performed either in tubes or in microtitration plates having multiple wells. For assays in plates, the wells will contain the specific amplification primers and control DNAs and the detection of amplification products will be automated. Reagents and amplification primers for universal bacterial detection will be included in kits for tests performed directly from clinical specimens. Components
 20 required for species-specific and genus-specific bacterial and/or fungal detection and identification as well as for the simultaneous antibiotic resistance genes detection will be included in kits for testing directly from bacterial or fungal cultures as well as in kits for testing directly from any type of clinical specimen.

The kits will be adapted for use with each type of specimen as described in
 25 example 16 for hybridization-based diagnostic kits.

EXAMPLE 18:

It is understood that the use of the probes and amplification primers described in this invention for bacterial and/or fungal detection and identification is not limited to clinical microbiology applications. In fact, we feel that other sectors could also benefit
 30 from these new technologies. For example, these tests could be used by industries for quality control of food, water, air, pharmaceutical products or other products requiring microbiological control. These tests could also be applied to detect and identify bacteria or fungi in biological samples from organisms other than humans (e.g. other primates, birds, plants, mammals, farm animals, livestock and others). These
 35 diagnostic tools could also be very useful for research purposes including clinical trials and epidemiological studies.

This invention has been described herein above, and it is readily apparent that modifications can be made thereto without departing from the spirit of this invention. These modifications are under the scope of this invention, as defined in the appended claims.

Table 1. Distribution (%) of nosocomial pathogens for various human infections in USA (1990-1992)¹.

| | Pathogen | UTI ² | SSI ³ | BSI ⁴ | Pneumonia | CSF ⁵ |
|----|-----------------------------------|------------------|------------------|------------------|-----------|------------------|
| 5 | <i>Escherichia coli</i> | 27 | 9 | 5 | 4 | 2 |
| | <i>Staphylococcus aureus</i> | 2 | 21 | 17 | 21 | 2 |
| | <i>Staphylococcus epidermidis</i> | 2 | 6 | 20 | 0 | 1 |
| | <i>Enterococcus faecalis</i> | 16 | 12 | 9 | 2 | 0 |
| | <i>Enterococcus faecium</i> | 1 | 1 | 0 | 0 | 0 |
| 10 | <i>Pseudomonas aeruginosa</i> | 12 | 9 | 3 | 18 | 0 |
| | <i>Klebsiella pneumoniae</i> | 7 | 3 | 4 | 9 | 0 |
| | <i>Proteus mirabilis</i> | 5 | 3 | 1 | 2 | 0 |
| | <i>Streptococcus pneumoniae</i> | 0 | 0 | 3 | 1 | 18 |
| | Group B <i>Streptococci</i> | 1 | 1 | 2 | 1 | 6 |
| 15 | Other <i>Streptococci</i> | 3 | 5 | 2 | 1 | 3 |
| | <i>Haemophilus influenzae</i> | 0 | 0 | 0 | 6 | 45 |
| | <i>Neisseria meningitidis</i> | 0 | 0 | 0 | 0 | 14 |
| | <i>Listeria monocytogenes</i> | 0 | 0 | 0 | 0 | 3 |
| | Other <i>Enterococci</i> | 1 | 1 | 0 | 0 | 0 |
| 20 | Other <i>Staphylococci</i> | 2 | | 8 | 13 | 20 |
| | <i>Candida albicans</i> | 9 | 3 | 5 | 5 | 0 |
| | Other <i>Candida</i> | 2 | | 1 | 3 | 10 |
| | <i>Enterobacter</i> spp. | 5 | 7 | 4 | 12 | 2 |
| | <i>Acinetobacter</i> spp. | 1 | 1 | 2 | 4 | 2 |
| 25 | <i>Citrobacter</i> spp. | 2 | 1 | 1 | 1 | 0 |
| | <i>Serratia marcescens</i> | 1 | 1 | 1 | 3 | 1 |
| | Other <i>Klebsiella</i> | 1 | 1 | 1 | 2 | 1 |
| | Others | 0 | 6 | 4 | 5 | 0 |

30 ¹ Data recorded by the National Nosocomial Infections Surveillance (NNIS) from 80 hospitals (Emori and Gaynes, 1993, Clin. Microbiol. Rev., 6:428-442).

² Urinary tract infection.

³ Surgical site infection.

⁴ Bloodstream infection.

35 ⁵ Cerebrospinal fluid.

Table 2. Distribution (%) of bloodstream infection pathogens in Quebec (1995), Canada (1992), UK (1969-1988) and USA (1990-1992).

| 5 | Organism | Quebec ¹ | Canada ² | UK ³ | | USA ⁴ |
|----|-----------------------------|---------------------|---------------------|--------------------|-------------------|-------------------|
| | | | | Community-acquired | Hospital-acquired | Hospital-acquired |
| | <i>E. coli</i> | 15.6 | 53.8 | 24.8 | 20.3 | 5.0 |
| | <i>S. epidermidis</i> | 25.8 | NI ⁶ | 0.5 | 7.2 | 31.0 |
| | and other CoNS ⁵ | | | | | |
| 10 | <i>S. aureus</i> | 9.6 | NI | 9.7 | 19.4 | 16.0 |
| | <i>S. pneumoniae</i> | 6.3 | NI | 22.5 | 2.2 | NR ⁷ |
| | <i>E. faecalis</i> | 3.0 | NI | 1.0 | 4.2 | NR |
| | <i>E. faecium</i> | 2.6 | NI | 0.2 | 0.5 | NR |
| | <i>Enterococcus</i> | NR | NI | NR | NR | 9.0 |
| 15 | spp. | | | | | |
| | <i>H. influenzae</i> | 1.5 | NR | 3.4 | 0.4 | NR |
| | <i>P. aeruginosa</i> | 1.5 | 8.2 | 1.0 | 8.2 | 3.0 |
| | <i>K. pneumoniae</i> | 3.0 | 11.2 | 3.0 | 9.2 | 4.0 |
| | <i>P. mirabilis</i> | NR | 3.9 | 2.8 | 5.3 | 1.0 |
| 20 | <i>S. pyogenes</i> | NR | NI | 1.9 | 0.9 | NR |
| | <i>Enterobacter</i> spp. | 4.1 | 5.5 | 0.5 | 2.3 | 4.0 |
| | <i>Candida</i> spp. | 8.5 | NI | NR | 1.0 | 8.0 |
| | Others | 18.5 | 17.4 ⁸ | 28.7 | 18.9 | 19.0 |

25 ¹ Data obtained for 270 isolates collected at the Centre Hospitalier de l'Université Laval (CHUL) during a 5 month period (May to October 1995).

² Data from 10 hospitals throughout Canada representing 941 gram-negative bacterial isolates. (Chamberland *et al.*, 1992, Clin. Infect. Dis., 15:615-628).

30 ³ Data from a 20-year study (1969-1988) for nearly 4000 isolates (Eykyn *et al.*, 1990, J. Antimicrob. Chemother., Suppl. C, 25:41-58).

⁴ Data recorded by the National Nosocomial Infections Surveillance (NNIS) from 80 hospitals (Emori and Gaynes, 1993, Clin. Microbiol. Rev., 6:428-442).

⁵ Coagulase-negative staphylococci.

⁶ NI, not included. This survey included only gram-negative species.

35 ⁷ NR, incidence not reported for these species or genera.

⁸ In this case, 17.4 stands for other gram-negative bacterial species.

Table 3. Distribution of positive and negative clinical specimens tested at the microbiology laboratory of the CHUL (February 1994 – January 1995).

| | Clinical specimens and/or sites | No. of samples tested (%) | % of positive specimens | % of negative specimens |
|----|------------------------------------|------------------------------|----------------------------|----------------------------|
| 5 | Urine | 17,981 (54.5) | 19.4 | 80.6 |
| | Blood culture/marrow | 10,010 (30.4) | 6.9 | 93.1 |
| | Sputum | 1,266 (3.8) | 68.4 | 31.6 |
| | Superficial pus | 1,136 (3.5) | 72.3 | 27.7 |
| 10 | Cerebrospinal fluid | 553 (1.7) | 1.0 | 99.0 |
| | Synovial fluid | 523 (1.6) | 2.7 | 97.3 |
| | Respiratory tract | 502 (1.5) | 56.6 | 43.4 |
| | Deep pus | 473 (1.4) | 56.8 | 43.2 |
| | Ears | 289 (0.9) | 47.1 | 52.9 |
| 15 | Pleural and pericardial fluid | 132 (0.4) | 1.0 | 99.0 |
| | Peritoneal fluid | 101(0.3) | 28.6 | 71.4 |
| | Total: | 32,966 (100.0) | 20.0 | 80.0 |

Table 4. Gram-negative bacterial species (90) used to test the specificity of PCR primers and DNA probes (continues on next page).

| | Bacterial species | Number of reference strains tested ^a | Bacterial species | Number of reference strains tested ^a |
|----|-----------------------------------|--|----------------------------------|--|
| 5 | <i>Acinetobacter baumannii</i> | 1 | <i>Moraxella phenylpyruvica</i> | 1 |
| | <i>Acinetobacter lwoffii</i> | 3 | <i>Morganella morganii</i> | 1 |
| | <i>Actinobacillus lignieresii</i> | 1 | <i>Neisseria animalis</i> | 1 |
| | <i>Alcaligenes faecalis</i> | 1 | <i>Neisseria canis</i> | 1 |
| | <i>Alcaligenes odorans</i> | 1 | <i>Neisseria caviae</i> | 1 |
| 10 | <i>Alcaligenes xylosoxydans</i> | | <i>Neisseria cinerea</i> | 1 |
| | subsp. <i>denitrificans</i> | 1 | <i>Neisseria cuniculi</i> | 1 |
| | <i>Bacteroides distasonis</i> | 1 | <i>Neisseria elongata</i> | 1 |
| | | | subsp. <i>elongata</i> | |
| | <i>Bacteroides fragilis</i> | 1 | <i>Neisseria elongata</i> | 1 |
| 15 | | | subsp. <i>glycoytica</i> | |
| | <i>Bacteroides ovatus</i> | 1 | <i>Neisseria flavescens</i> | 1 |
| | <i>Bacteroides</i> | 1 | <i>Neisseria flavescens</i> | 1 |
| | <i>thetaiotaomicron</i> | | <i>Branham</i> | |
| | <i>Bacteroides vulgatus</i> | 1 | <i>Neisseria gonorrhoeae</i> | 18 |
| 20 | <i>Bordetella bronchiseptica</i> | 1 | <i>Neisseria lactamica</i> | 1 |
| | <i>Bordetella parapertussis</i> | 1 | <i>Neisseria meningitidis</i> | 4 |
| | <i>Bordetella pertussis</i> | 2 | <i>Neisseria mucosa</i> | 2 |
| | <i>Burkholderia cepacia</i> | 1 | <i>Neisseria polysaccharea</i> | 1 |
| | <i>Citrobacter amalonaticus</i> | 1 | <i>Neisseria sicca</i> | 3 |
| 25 | <i>Citrobacter diversus</i> | 2 | <i>Neisseria subflava</i> | 3 |
| | subsp. <i>koseri</i> | | | |
| | <i>Citrobacter freundii</i> | 1 | <i>Neisseria weaveri</i> | 1 |
| | <i>Comamonas acidovorans</i> | 1 | <i>Ochrobactrum antropi</i> | 1 |
| | <i>Enterobacter aerogenes</i> | 1 | <i>Pasteurella aerogenes</i> | 1 |
| 30 | <i>Enterobacter</i> | 1 | <i>Pasteurella multocida</i> | 1 |
| | <i>agglomerans</i> | | | |
| | <i>Enterobacter cloacae</i> | 1 | <i>Prevotella melaninogenica</i> | 1 |
| | <i>Escherichia coli</i> | 9 | <i>Proteus mirabilis</i> | 3 |
| | <i>Escherichia fergusonii</i> | 1 | <i>Proteus vulgaris</i> | 1 |

| | Bacterial species | Number of reference strains tested ^a | Bacterial species | Number of reference strains tested ^a |
|----|---------------------------------------|--|-------------------------------------|--|
| | <i>Escherichia hermannii</i> | 1 | <i>Providencia alcalifaciens</i> | 1 |
| | <i>Escherichia vulneris</i> | 1 | <i>Providencia rettgeri</i> | 1 |
| | <i>Flavobacterium meningosepticum</i> | 1 | <i>Providencia rustigianii</i> | 1 |
| 5 | <i>Flavobacterium indologenes</i> | 1 | <i>Providencia stuartii</i> | 1 |
| | <i>Flavobacterium odoratum</i> | 1 | <i>Pseudomonas aeruginosa</i> | 14 |
| | <i>Fusobacterium necrophorum</i> | 2 | <i>Pseudomonas fluorescens</i> | 2 |
| 10 | <i>Gardnerella vaginalis</i> | 1 | <i>Pseudomonas stutzeri</i> | 1 |
| | <i>Haemophilus haemolyticus</i> | 1 | <i>Salmonella arizonae</i> | 1 |
| | <i>Haemophilus influenzae</i> | 12 | <i>Salmonella choleraesuis</i> | 1 |
| | <i>Haemophilus parahaemolyticus</i> | 1 | <i>Salmonella gallinarum</i> | 1 |
| 15 | <i>Haemophilus parainfluenzae</i> | 2 | <i>Salmonella typhimurium</i> | 3 |
| | <i>Hafnia alvei</i> | 1 | <i>Serratia liquefaciens</i> | 1 |
| | <i>Kingella indologenes</i> | 1 | <i>Serratia marcescens</i> | 1 |
| 20 | subsp. <i>suttonella</i> | | | |
| | <i>Kingella kingae</i> | 1 | <i>Shewanella putida</i> | 1 |
| | <i>Klebsiella ornithinolytica</i> | 1 | <i>Shigella boydii</i> | 1 |
| | <i>Klebsiella oxytoca</i> | 1 | <i>Shigella dysenteriae</i> | 1 |
| | <i>Klebsiella pneumoniae</i> | 8 | <i>Shigella flexneri</i> | 1 |
| 25 | <i>Moraxella atlantae</i> | 1 | <i>Shigella sonnei</i> | 1 |
| | <i>Moraxella catarrhalis</i> | 5 | <i>Stenotrophomonas maltophilia</i> | 1 |
| | <i>Moraxella lacunata</i> | 1 | <i>Yersinia enterocolitica</i> | 1 |
| | <i>Moraxella osloensis</i> | 1 | | |

- 30 ^a Most reference strains were obtained from the American Type Culture Collection (ATCC). The other reference strains were obtained from (i) the Laboratoire de Santé Publique du Québec (LSPQ), (ii) the Center for Disease Control and Prevention (CDC) and (iii) the National Culture Type Collection (NCTC).

Table 5. Gram-positive bacterial species (97) used to test the specificity of PCR primers and DNA probes (continues on next page).

| | Bacterial species | Number of reference strains tested ^a | Bacterial species | Number of reference strains tested ^a |
|----|---|--|--|--|
| 5 | <i>Abiotrophia adiacens</i> | 1 | <i>Micrococcus kristinae</i> | 1 |
| | <i>Abiotrophia defectiva</i> | 1 | <i>Micrococcus luteus</i> | 1 |
| | <i>Actinomyces israelii</i> | 1 | <i>Micrococcus lylae</i> | 1 |
| | <i>Clostridium perfringens</i> | 1 | <i>Micrococcus roseus</i> | 1 |
| | <i>Corynebacterium accolens</i> | 1 | <i>Micrococcus varians</i> | 1 |
| 10 | <i>Corynebacterium</i> <i>aquaticum</i> | 1 | <i>Peptococcus niger</i> | 1 |
| | <i>Corynebacterium bovis</i> | 1 | <i>Peptostreptococcus</i> <i>anaerobius</i> | 1 |
| | <i>Corynebacterium cervicis</i> | 1 | <i>Peptostreptococcus</i> <i>asaccharolyticus</i> | 1 |
| | <i>Corynebacterium</i> <i>diphtheriae</i> | 6 | <i>Staphylococcus aureus</i> | 10 |
| 15 | <i>Corynebacterium</i> <i>flavescens</i> | 1 | <i>Staphylococcus auricularis</i> | 1 |
| | <i>Corynebacterium</i> <i>genitalium</i> | 6 | <i>Staphylococcus capitis</i> subsp. <i>urealyticus</i> | 1 |
| 20 | <i>Corynebacterium jeikeium</i> | 1 | <i>Staphylococcus cohnii</i> | 1 |
| | <i>Corynebacterium kutcheri</i> | 1 | <i>Staphylococcus epidermidis</i> | 2 |
| | <i>Corynebacterium</i> <i>matruchotii</i> | 1 | <i>Staphylococcus</i> <i>haemolyticus</i> | 2 |
| | <i>Corynebacterium</i> <i>minutissimum</i> | 1 | <i>Staphylococcus hominis</i> | 2 |
| 25 | <i>Corynebacterium</i> <i>mycetoides</i> | 1 | <i>Staphylococcus</i> <i>lugdunensis</i> | 1 |
| | <i>Corynebacterium</i> <i>pseudodiphtheriticum</i> | 1 | <i>Staphylococcus</i> <i>saprophyticus</i> | 3 |
| 30 | <i>Corynebacterium</i> <i>pseudogenitalium</i> | 6 | <i>Staphylococcus schleiferi</i> | 1 |
| | <i>Corynebacterium renale</i> | 1 | <i>Staphylococcus sciuri</i> | 1 |
| | <i>Corynebacterium striatum</i> | 1 | <i>Staphylococcus simulans</i> | 1 |
| | <i>Corynebacterium ulcerans</i> | 1 | <i>Staphylococcus warneri</i> | 1 |

| | Bacterial species | Number of reference strains tested ^a | Bacterial species | Number of reference strains tested ^a |
|----|-------------------------------------|--|-----------------------------------|--|
| | <i>Corynebacterium urealyticum</i> | 1 | <i>Staphylococcus xylosus</i> | 1 |
| | <i>Corynebacterium xerosis</i> | 1 | <i>Streptococcus agalactiae</i> | 6 |
| | <i>Enterococcus avium</i> | 1 | <i>Streptococcus anginosus</i> | 2 |
| 5 | <i>Enterococcus casseliflavus</i> | 1 | <i>Streptococcus bovis</i> | 2 |
| | <i>Enterococcus cecorum</i> | 1 | <i>Streptococcus constellatus</i> | 1 |
| | <i>Enterococcus dispar</i> | 1 | <i>Streptococcus crista</i> | 1 |
| | <i>Enterococcus durans</i> | 1 | <i>Streptococcus dysgalactiae</i> | 1 |
| 10 | <i>Enterococcus faecalis</i> | 6 | <i>Streptococcus equi</i> | 1 |
| | <i>Enterococcus faecium</i> | 3 | <i>Streptococcus gordonii</i> | 1 |
| | <i>Enterococcus flavescens</i> | 1 | Group C <i>Streptococci</i> | 1 |
| | <i>Enterococcus gallinarum</i> | 3 | Group D <i>Streptococci</i> | 1 |
| | <i>Enterococcus hirae</i> | 1 | Group E <i>Streptococci</i> | 1 |
| 15 | <i>Enterococcus mundtii</i> | 1 | Group F <i>Streptococci</i> | 1 |
| | <i>Enterococcus pseudoavium</i> | 1 | Group G <i>Streptococci</i> | 1 |
| | <i>Enterococcus raffinosus</i> | 1 | <i>Streptococcus intermedius</i> | 1 |
| | <i>Enterococcus saccharolyticus</i> | 1 | <i>Streptococcus mitis</i> | 2 |
| 20 | <i>Enterococcus solitarius</i> | 1 | <i>Streptococcus mutans</i> | 1 |
| | <i>Eubacterium lentum</i> | 1 | <i>Streptococcus oralis</i> | 1 |
| | <i>Gemella haemolysans</i> | 1 | <i>Streptococcus parasanguis</i> | 1 |
| | <i>Gemella morbillorum</i> | 1 | <i>Streptococcus pneumoniae</i> | 6 |
| 25 | <i>Lactobacillus acidophilus</i> | 1 | <i>Streptococcus pyogenes</i> | 3 |
| | <i>Listeria innocua</i> | 1 | <i>Streptococcus salivarius</i> | 2 |
| | <i>Listeria ivanovii</i> | 1 | <i>Streptococcus sanguis</i> | 2 |
| | <i>Listeria grayi</i> | 1 | <i>Streptococcus sobrinus</i> | 1 |
| | <i>Listeria monocytogenes</i> | 3 | <i>Streptococcus suis</i> | 1 |
| 30 | <i>Listeria murrayi</i> | 1 | <i>Streptococcus uberis</i> | 1 |
| | <i>Listeria seeligeri</i> | 1 | <i>Streptococcus vestibularis</i> | 1 |
| | <i>Listeria welshimeri</i> | 1 | | |

^a Most reference strains were obtained from the American Type Culture Collection (ATCC). The other reference strains were obtained from (i) the Laboratoire de Santé Publique du Québec (LSPQ), (ii) the Center for Disease Control and Prevention (CDC) and (iii) the National Culture Type Collection (NCTC).

Table 6. Fungal species (12) used to test the specificity of PCR primers and DNA probes.

| | Fungal species | Number of reference strains tested ^a |
|----|---------------------------------|---|
| 5 | <i>Candida albicans</i> | 12 |
| | <i>Candida glabrata</i> | 1 |
| | <i>Candida guilliermondii</i> | 1 |
| | <i>Candida kefyr</i> | 3 |
| 10 | <i>Candida krusei</i> | 2 |
| | <i>Candida lusitanae</i> | 1 |
| | <i>Candida parapsilosis</i> | 2 |
| | <i>Candida tropicalis</i> | 3 |
| | <i>Rhodotorula glutinis</i> | 1 |
| 15 | <i>Rhodotorula minuta</i> | 1 |
| | <i>Rhodotorula rubra</i> | 1 |
| | <i>Saccharomyces cerevisiae</i> | 1 |

^a Most reference strains were obtained from (i) the American Type Culture Collection (ATCC) and (ii) the Laboratoire de Santé Publique du Québec (LSPQ).

Table 7. PCR assays developed for several clinically important bacterial and fungal pathogens (continues on next page).

| | Organism | Primer Pair ^a | Amplicon | Ubiquity ^b | DNA amplification from | |
|----|--|--------------------------|-----------|-----------------------|------------------------|------------------------|
| | | SEQ ID NO | size (bp) | | culture ^c | specimens ^d |
| | <i>Enterococcus faecium</i> | 1-2 | 216 | 79/80 | + | + |
| 5 | <i>Listeria monocytogenes</i> | 3-4 | 130 | 164/168 ^e | + | + |
| | <i>Neisseria meningitidis</i> | 5-6 | 177 | 258/258 | + | + |
| | <i>Staphylococcus saprophyticus</i> | 7-8 | 149 | 245/260 | + | NT |
| 10 | <i>Streptococcus agalactiae</i> | 9-10 | 154 | 29/29 | + | + |
| | <i>Candida albicans</i> | 11-12 | 149 | 88/88 | + | NT |
| | <i>Enterococcus</i> spp. (11 species) ^f | 13-14 | 112 | 87/87 | + | NT |
| 15 | <i>Neisseria</i> spp. (12 species) ^f | 15-16 | 103 | 321/321 | + | + |
| | <i>Staphylococcus</i> spp. (14 species) | 17-18 | 192 | 13/14 | + | NT |
| | | 19-20 | 221 | 13/14 | + | NT |
| 20 | <i>Streptococcus</i> spp. (22 species) ^f | 21-22 | 153 | 210/214 ^g | + | + |
| | Universal detection ^h (95 species) ⁱ | 23-24 | 309 | 104/ 116 ⁱ | + | + |

^a All primer pairs are specific in PCR assays since no amplification was observed with DNA from the bacterial and fungal species other than the species of interest listed in Tables 4, 5 and 6.

^b Ubiquity was tested by using reference strains as well as strains from throughout the world, which are representative of the diversity within each target species or genus.

^c For all primer pairs, PCR amplifications performed directly from a standardized microbial suspension (MacFarland) or from a colony were all specific and ubiquitous.

^d PCR assays performed directly from blood cultures, urine specimens or

cerebrospinal fluid. NT, not tested.

- ° The four *L. monocytogenes* strains undetected are not clinical isolates. These strains were isolated from food and are not associated with a human infection.
- † The bacterial species tested include all those clinically relevant for each genus (Tables 4 and 5). All of these species were efficiently amplified by their respective genus-specific PCR assay, except for the *Staphylococcus*-specific assay, which does not amplify *S. sciuri*.
- ° The *Streptococcus*-specific PCR assay did not amplify 3 out of 9 strains of *S. mutans* and 1 out of 3 strains of *S. salivarius*.
- h The primers selected for universal bacterial detection do not amplify DNA of non-bacterial origin, including human and other types of eukaryotic genomic DNA.
- † For the universal amplification, the 95 bacterial species tested represent the most clinically important bacterial species listed in Tables 4 and 5. The 12 strains not amplified are representatives of genera *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species).

Table 8. Target genes for the various genus-specific, species-specific and universal amplification assays.

| 20 | Microorganisms | Gene | Protein encoded |
|----|-------------------------------------|-------------|-------------------------------------|
| | <i>Candida albicans</i> | <i>tuf</i> | translation elongation factor EF-Tu |
| | <i>Enterococcus faecium</i> | <i>ddl</i> | D-alanine:D-alanine ligase |
| | <i>Listeria monocytogenes</i> | <i>actA</i> | actin-assembly inducing protein |
| | <i>Neisseria meningitidis</i> | <i>omp</i> | outer membrane protein |
| 25 | <i>Streptococcus agalactiae</i> | <i>cAMP</i> | cAMP factor |
| | <i>Staphylococcus saprophyticus</i> | unknown | unknown |
| | <i>Enterococcus</i> spp. | <i>tuf</i> | translation elongation factor EF-Tu |
| | <i>Neisseria</i> spp. | <i>asd</i> | ASA-dehydrogenase |
| 30 | <i>Staphylococcus</i> spp. | <i>tuf</i> | translation elongation factor EF-Tu |
| | <i>Streptococcus</i> spp. | <i>recA</i> | RecA protein |
| | Universal detection | <i>tuf</i> | translation elongation factor EF-Tu |

Table 9. Antibiotic resistance genes selected for diagnostic purposes.

| | Genes | SEQ ID NOs | | Antibiotics | Bacteria ^a |
|----|--------------------------|------------------|----------------------|-----------------|--|
| | | selected primers | originating fragment | | |
| 5 | <i>bla_{oxa}</i> | 49-50 | 110 | β-lactams | <i>Enterobacteriaceae</i> , <i>Pseudomonadaceae</i> |
| | <i>blaZ</i> | 51-52 | 111 | β-lactams | <i>Enterococcus</i> spp. |
| | <i>aac6'-IIa</i> | 61-64 | 112 | Aminoglycosides | <i>Pseudomonadaceae</i> |
| | <i>ermA</i> | 91-92 | 113 | Macrolides | <i>Staphylococcus</i> spp. |
| 10 | <i>ermB</i> | 93-94 | 114 | Macrolides | <i>Staphylococcus</i> spp. |
| | <i>ermC</i> | 95-96 | 115 | Macrolides | <i>Staphylococcus</i> spp. |
| | <i>vanB</i> | 71-74 | 116 | Vancomycin | <i>Enterococcus</i> spp. |
| | <i>vanC</i> | 75-76 | 117 | Vancomycin | <i>Enterococcus</i> spp. |
| 15 | <i>aad(6')</i> | 173-174 | - | Streptomycin | <i>Enterococcus</i> spp. |

^a Bacteria having high incidence for the specified antibiotic resistance genes. The presence of these antibiotic resistance genes in other bacteria is not excluded.

Table 10. Antibiotic resistance genes from our co-pending US (N.S. 08/526840) and PCT (PCT/CA/95/00528) patent applications for which we have selected PCR primer pairs.

| 5 | Genes | SEQ ID NOs | Antibiotics | Bacteria ^a |
|----|--------------------------|------------|--|---|
| | of selected primers | | | |
| | <i>bla_{tem}</i> | 37-40 | β-lactams | <i>Enterobacteriaceae</i> , <i>Pseudomonadaceae</i> , <i>Haemophilus</i> spp., <i>Neisseria</i> spp. |
| | <i>bla_{rob}</i> | 45-48 | β-lactams | <i>Haemophilus</i> spp., <i>Pasteurella</i> spp. |
| 10 | <i>bla_{shv}</i> | 41-44 | β-lactams | <i>Klebsiella</i> spp. and other <i>Enterobacteriaceae</i> |
| | <i>aadB</i> | 53-54 | Aminoglycosides | <i>Enterobacteriaceae</i> , <i>Pseudomonadaceae</i> |
| | <i>aacC1</i> | 55-56 | | |
| | <i>aacC2</i> | 57-58 | | |
| 15 | <i>aacC3</i> | 59-60 | | |
| | <i>aacA4</i> | 65-66 | | |
| | <i>mecA</i> | 97-98 | β-lactams | <i>Staphylococcus</i> spp. |
| | <i>vanA</i> | 67-70 | Vancomycin | <i>Enterococcus</i> spp. |
| | <i>satA</i> | 81-82 | Macrolides | <i>Enterococcus</i> spp. |
| 20 | <i>aac(6')-aph(2'')</i> | 83-86 | Aminoglycosides | <i>Enterococcus</i> spp., <i>Staphylococcus</i> spp. |
| | <i>vat</i> | 87-88 | Macrolides | <i>Staphylococcus</i> spp. |
| | <i>vga</i> | 89-90 | Macrolides | <i>Staphylococcus</i> spp. |
| | <i>msrA</i> | 77-80 | Erythromycin | <i>Staphylococcus</i> spp. |
| | <i>int</i> | 99-102 | β-lactams, | <i>Enterobacteriaceae</i> , |
| 25 | | | trimethoprim, | |
| | <i>sul</i> | 103-106 | aminoglycosides, antiseptic, chloramphenicol | <i>Pseudomonadaceae</i> |

^a Bacteria having high incidence for the specified antibiotic resistance genes. The presence of these antibiotic resistance genes in other bacteria is not excluded.

Table 11. Correlation between disk diffusion and PCR amplification of antibiotic resistance genes in *Staphylococcus* species^a.

| 5 | Antibiotic | Phenotype | PCR | Disk diffusion (Kirby-Bauer) ^b | | |
|----|--------------|-------------------------|-----|---|--------------|-----------|
| | | | | Resistant | Intermediate | Sensitive |
| 5 | Penicillin | <i>blaZ</i> | + | 165 | 0 | 0 |
| | | | - | 0 | 0 | 31 |
| | Oxacillin | <i>mecA</i> | + | 51 | 11 | 4 |
| | | | - | 2 | 0 | 128 |
| | Gentamycin | <i>aac(6'')aph(2'')</i> | + | 24 | 18 | 6 |
| | | | - | 0 | 0 | 148 |
| 10 | Erythromycin | <i>ermA</i> | + | 15 | 0 | 0 |
| | | <i>ermB</i> | + | 0 | 0 | 0 |
| | | <i>ermC</i> | + | 43 | 0 | 0 |
| | | <i>msrA</i> | + | 4 | 0 | 0 |
| 15 | | | + | 4 | 0 | 0 |
| | | | - | 0 | 1 | 136 |

^a The *Staphylococcus* strains studied include *S. aureus* (82 strains), *S. epidermidis* (83 strains), *S. hominis* (2 strains), *S. capitis* (3 strains), *S. haemolyticus* (9 strains), *S. simulans* (12 strains) and *S. warneri* (5 strains), for a total of 196 strains.

^b Susceptibility testing was performed by the method of Kirby-Bauer according to the protocol recommended by the National Committee of Clinical Laboratory Standards (NCCLS).

Table 12. Correlation between disk diffusion profiles and PCR amplification of antibiotic resistance genes in *Enterococcus* species^a.

| | Antibiotic | Phenotype | PCR | Disk diffusion (Kirby-Bauer) ^b | |
|----|--------------|------------------------|-----|---|-----------|
| | | | | Resistant | Sensitive |
| 5 | Ampicillin | <i>blaZ</i> | + | 0 | 2 |
| | | | - | 1 | 30 |
| | Gentamycin | <i>aac(6')aph(2'')</i> | + | 51 | 1 |
| | | | - | 3 | 38 |
| 10 | Streptomycin | <i>aad(6'')</i> | + | 26 | 15 |
| | | | - | 6 | 27 |
| | Vancomycin | <i>vanA</i> | + | 36 | 0 |
| | | <i>vanB</i> | + | 26 | 0 |
| | | | - | 0 | 40 |
| 15 | | | | | |

^a The *Enterococcus* strains studied include *E. faecalis* (33 strains) and *E. faecium* (69 strains), for a total of 102 strains.

^b Susceptibility testing was performed by the method of Kirby-Bauer according to the protocol recommended by the National Committee of Clinical Laboratory Standards (NCCLS).

Table 13. Origin of *tuf* sequences in the Sequence Listing (continues on next page).

| | SEQ ID NO | Bacterial or fungal species | Source |
|----|-----------|---|-------------|
| 5 | 118 | <i>Abiotrophia adiacens</i> | This patent |
| | 119 | <i>Abiotrophia defectiva</i> | This patent |
| | 120 | <i>Candida albicans</i> | This patent |
| | 121 | <i>Candida glabrata</i> | This patent |
| | 122 | <i>Candida krusei</i> | This patent |
| 10 | 123 | <i>Candida parapsilosis</i> | This patent |
| | 124 | <i>Candida tropicalis</i> | This patent |
| | 125 | <i>Corynebacterium accolens</i> | This patent |
| | 126 | <i>Corynebacterium diphtheriae</i> | This patent |
| | 127 | <i>Corynebacterium genitalium</i> | This patent |
| 15 | 128 | <i>Corynebacterium jeikeium</i> | This patent |
| | 129 | <i>Corynebacterium pseudotuberculosis</i> | This patent |
| | 130 | <i>Corynebacterium striatum</i> | This patent |
| | 131 | <i>Enterococcus avium</i> | This patent |
| | 132 | <i>Enterococcus faecalis</i> | This patent |
| 20 | 133 | <i>Enterococcus faecium</i> | This patent |
| | 134 | <i>Enterococcus gallinarum</i> | This patent |
| | 135 | <i>Gardnerella vaginalis</i> | This patent |
| | 136 | <i>Listeria innocua</i> | This patent |
| | 137 | <i>Listeria ivanovii</i> | This patent |
| 25 | 138 | <i>Listeria monocytogenes</i> | This patent |
| | 139 | <i>Listeria seeligeri</i> | This patent |
| | 140 | <i>Staphylococcus aureus</i> | This patent |
| | 141 | <i>Staphylococcus epidermidis</i> | This patent |
| | 142 | <i>Staphylococcus saprophyticus</i> | This patent |
| 30 | 143 | <i>Staphylococcus simulans</i> | This patent |
| | 144 | <i>Streptococcus agalactiae</i> | This patent |
| | 145 | <i>Streptococcus pneumoniae</i> | This patent |

| | SEQ ID NO | Bacterial or fungal species | Source |
|----|-----------|-----------------------------------|-------------|
| | 146 | <i>Streptococcus salivarius</i> | This patent |
| | 147 | <i>Agrobacterium tumefaciens</i> | Database |
| | 148 | <i>Bacillus subtilis</i> | Database |
| | 149 | <i>Bacteroides fragilis</i> | Database |
| 5 | 150 | <i>Borrelia burgdorferi</i> | Database |
| | 151 | <i>Brevibacterium linens</i> | Database |
| | 152 | <i>Burkholderia cepacia</i> | Database |
| | 153 | <i>Chlamydia trachomatis</i> | Database |
| | 154 | <i>Escherichia coli</i> | Database |
| 10 | 155 | <i>Fibrobacter succinogenes</i> | Database |
| | 156 | <i>Flavobacterium ferrugineum</i> | Database |
| | 157 | <i>Haemophilus influenzae</i> | Database |
| | 158 | <i>Helicobacter pylori</i> | Database |
| | 159 | <i>Micrococcus luteus</i> | Database |
| 15 | 160 | <i>Mycobacterium tuberculosis</i> | Database |
| | 161 | <i>Mycoplasma genitalium</i> | Database |
| | 162 | <i>Neisseria gonorrhoeae</i> | Database |
| | 163 | <i>Rickettsia prowazekii</i> | Database |
| | 164 | <i>Salmonella typhimurium</i> | Database |
| 20 | 165 | <i>Shewanella putida</i> | Database |
| | 166 | <i>Stigmatella aurantiaca</i> | Database |
| | 167 | <i>Streptococcus pyogenes</i> | Database |
| | 168 | <i>Thiobacillus cuprinus</i> | Database |
| | 169 | <i>Treponema pallidum</i> | Database |
| 25 | 170 | <i>Ureaplasma urealyticum</i> | Database |
| | 171 | <i>Wolinella succinogenes</i> | Database |

Annex I: Strategy for the selection from *tuf* sequences of the universal amplification primers (continues on pages 49 to 51).

| | | SEQ ID |
|----|------------------------|--------|
| | | NO |
| 5 | <i>Abiotrophia</i> | 118 |
| | <i>adiacens</i> | |
| | <i>Abiotrophia</i> | 119 |
| | <i>defectiva</i> | |
| | <i>Agrobacterium</i> | 147 |
| 10 | <i>tumefaciens</i> | |
| | <i>Bacillus</i> | 148 |
| | <i>subtilis</i> | |
| | <i>Bacteroides</i> | 149 |
| | <i>fragilis</i> | |
| 15 | <i>Borrelia</i> | 150 |
| | <i>burgdorferi</i> | |
| | <i>Brevibacterium</i> | 151 |
| | <i>linens</i> | |
| | <i>Burkholderia</i> | 152 |
| 20 | <i>cepacia</i> | |
| | <i>Chlamydia</i> | 153 |
| | <i>trachomatis</i> | |
| | <i>Corynebacterium</i> | 126 |
| | <i>diphtheriae</i> | |

| | | | |
|----|-----------------------------------|--|-----|
| 5 | <i>Corynebacterium genitalium</i> | CCACCGTTAC CTCCATCGAG ATGTTCA...AGATGGT TATGCCGGGC GACAACGTTG | 127 |
| | <i>Corynebacterium jeikeium</i> | CCACCGTTAC CTCCATCGAG ATGTTCA...AGATGGT TATGCCGGGC GACAACGTTG | 128 |
| 10 | <i>Enterococcus faecalis</i> | CAACYGTTAC AGGTGTTGAA ATGTTCC...AAATGGT AATGCCCTGGT GATAACGTTG | 132 |
| | <i>Enterococcus faecium</i> | CAACAGTTAC TGGTGTGAA ATGTTCC...AAATGGT CATGCCCGGT GACAACGT.. | 133 |
| 15 | <i>Escherichia coli</i> | CTACCTGTAC TGGCGTTGAA ATGTTCC...AGATGGT AATGCCGGGC GACAACATCA | 154 |
| | <i>Fibrobacter succinogenes</i> | ACGTCAATCAC CGGTGTTGAA ATGTTCC...AAATGGT TACTCCGGGT GACACGGTCA | 155 |
| 20 | <i>Flavobacterium ferrugineum</i> | CTACCGTTAC AGGTGTTGAG ATGTTCC...AAATGGT TATGCCCTGGT GATAACACCA | 156 |
| | <i>Gardnerella vaginalis</i> | CCACCGTCAC CTCTATCGAG ACCTTCC...AAATGGT TCAGCCAGGC GATCAGCGAA | 135 |
| 25 | <i>Haemophilus influenzae</i> | CTACTGTAAC GGGTGTGAA ATGTTCC...AAATGGT AATGCCAGGC GATAACATCA | 157 |
| | <i>Helicobacter pylori</i> | CGACTGTAAC CGGTGTAGAA ATGTTTA...AAATGGT TATGCCCTGGC GATAATGTGA | 158 |
| 30 | <i>Listeria monocytogenes</i> | TAGTAGTAAC TGGAGTAGAA ATGTTCC...AAATGGT AATGCCCTGGT GATAACATTG | 138 |
| | <i>Micrococcus luteus</i> | CCACTGTAC CGGCATCGAG ATGTTCC...AGATGGT CATGCCCGGC GACAACACCG | 159 |
| 35 | <i>Mycobacterium tuberculosis</i> | CCACCGTCAC CGGTGTGAG ATGTTCC...AGATGGT GATGCCCGGT GACAACACCA | 160 |

| | |
|-----|---|
| 161 | <u>GAGTGTGTAC</u> <u>TGGATATGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>TCTACCTGGT</u> <u>GATAATGCTT</u> |
| 162 | <u>CCACCTGTAC</u> <u>CGGCGTTGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>AATGCCGGGT</u> <u>GAGAACGTAA</u> |
| 163 | <u>CGACTGTGTAC</u> <u>AGGTGTAGAA</u> <u>ATGTTC...</u> <u>AGATGGT</u> <u>TATGCCCTGGA</u> <u>GATAATGCTA</u> |
| 164 | <u>CTACCTGTAC</u> <u>TGGCGTTGAA</u> <u>ATGTTC...</u> <u>AGATGGT</u> <u>AATGCCGGGC</u> <u>GACAACATCA</u> |
| 165 | <u>CAACGTGTAC</u> <u>TGGTGTAGAA</u> <u>ATGTTC...</u> <u>AGATGGT</u> <u>AATGCCAGGC</u> <u>GATAACATCA</u> |
| 166 | <u>CGGTCAATAC</u> <u>GGGGTGGAG</u> <u>ATGTTC...</u> <u>AGATGGT</u> <u>GATGCCGGGA</u> <u>GACAACATCG</u> |
| 140 | <u>CAACTGTGTAC</u> <u>AGGTGTAGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>AATGCCCTGGT</u> <u>GATAACGTTG</u> |
| 141 | <u>CAACTGTGTAC</u> <u>TGGTGTAGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>TATGCCCTGGC</u> <u>GACAACGTTG</u> |
| 144 | <u>CAGTGTGTAC</u> <u>TGGTGTAGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>TATGCCCTGGT</u> <u>GATAACGTTA</u> |
| 145 | <u>CAGTGTGTAC</u> <u>TGGTGTAGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>AATGCCCTGGT</u> <u>GATAACGTGA</u> |
| 167 | <u>CTGTGTGTAC</u> <u>TGGTGTAGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>TATGCCCTGGT</u> <u>GATAACGTGA</u> |
| 168 | <u>CCACCTGCAC</u> <u>CGGCGTGGAA</u> <u>ATGTTC...</u> <u>AAATGGT</u> <u>CATGCCCGGC</u> <u>GATAATGTGA</u> |
| 169 | <u>CAGTGTGTAC</u> <u>TGGCATTTAG</u> <u>ATGTTTA...</u> <u>ACATGGT</u> <u>GAAGCCGGGG</u> <u>GATAACACCA</u> |

| | | |
|--------------------------|---|----------------------------|
| Ureaplasma | CTGTTGTTAC AGGAATTGAA ATGTTTA...ATTGGT TATGCCAGGT <u>GATGACGTTG</u> | 170 |
| urealyticum | | |
| Molinitella | CAACCGTAAC TGGCGTTGAG ATGTTCC...AGATGGT TATGCCCTGGT <u>GACAACGTTA</u> | 171 |
| succinogenes | | |
| 5 Candida | GTGTTACCAC TGAAGTCAAR TCCGTTG...AGRAATT GGAAGAAAT CCAAAATTCG | 120 |
| albicans | | |
| Schizo- | GTGTCACTAC CGAAGTCAAG TCTGTTG...AGAAGAT TGAGGAGTCC CTTAAGTTTG | |
| saccharomyces pombe | | |
| Human | TGACAGGCAT TGAGATGTTT CACAAGA...AGAAGAGCTTGCCATG CCGGGGGAGG | |
| 10 Selected ^a | ACIKKIAC IGGIGTIGAR ATGTT ATGGT <u>IATGCCIGGI</u> GAIAAYRT | |
| equences ^a | | |
| Selected | SEQ ID NO: 23 | SEQ ID NO: 24 ^b |
| universal | | |
| 15 primer | ACIKKIAC IGGIGTIGAR ATGTT | AYRTT ITCICCIIGC ATIACCAT |
| sequences ^a : | | |

The sequence numbering refers to the *E. coli* *tuf* gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

20 ^a "I" stands for inosine which is a nucleotide analog that can bind to any of the four nucleotides A, C, G or T. "K", "R" and "Y" designate nucleotide positions which are degenerated. "K" stands for T or G; "R" stands for A or G; "Y" stands for C or T.

^b This sequence is the reverse complement of the above *tuf* sequence.

Annex II: Strategy for the selection from *tuf* sequences of the amplification primers specific for the genus *Enterococcus* (continues on pages 53 and 54).

| | 314 | 348 | 401 | 435 | SEQ ID NO |
|-----------------------------------|---|-----|-----|-----|--------------|
| 5 <i>Bacillus subtilis</i> | <u>CGCGACACTG AAAAACCATT CATGATGCCA GTTGA...CGCGG ACAAGTTAAA GTCGGTGACG AAGTTGAAAT</u> | | | | 148 |
| <i>Bacteroides fragilis</i> | <u>CGCGATGTTG ATAAACCTTT CTTGATGCCG GTAGA...ACTGG TGTATATCCAT GTAGGTGATG AAATCGAAAT</u> | | | | 149 |
| <i>Burkholderia cepacia</i> | <u>CGTGCAGTTG ACGGCGCGTT CCTGATGCCG GTGGA...CGCGG CATCGTGAAG GTCGGCGAAG AAATCGAAAT</u> | | | | 152 |
| <i>Chlamydia trachomatis</i> | <u>AGAGAAATTG ACAAGCCTTT CTTAATGCCCT ATTGA...CGTGG AATTGTTAAA GTTCCGATA AAGTTCAGTT</u> | | | | 153 |
| <i>Corynebacterium diptheriae</i> | <u>CGTGAGACCG ACAAGCCATT CCTCATGCCCT ATCGA...CGTGG CTCCCTGAAG GTCAACGAGG ACGTCGAGAT</u> | | | | 126 |
| 15 <i>Enterococcus avium</i> | <u>CGTGATACTG ACAAACCAAT CATGATGCCA GTCGA...CGTGG ACAAGTTCGC GTTGGTGACG AAGTTGAAAT</u> | | | | 131 |
| <i>Enterococcus faecalis</i> | <u>CGTGATACTG ACAAACCAAT CATGATGCCA GTCGA...CGTGG TGAAGTTCGC GTTGGTGACG AAGTTGAAAT</u> | | | | 132 |
| <i>Enterococcus faecium</i> | <u>CGTGACAACG ACAAACCAAT CATGATGCCA GTTGA...CGTGG ACAAGTTCGC GTTGGTGACG AAGTTGAAAT</u> | | | | 133 |
| 20 <i>Enterococcus gallinarum</i> | <u>CGTGATACTG ACAAACCAAT CATGATGCCA GTCGA...CGTGG ACAAGTTCGC GTTGGTGATG AAGTAGAAAT</u> | | | | 134 |
| <i>Escherichia coli</i> | <u>CGTCCGATTG ACAAGCCGTT CCTGCTGCCG ATCGA...CGCGG TATCATCAAA GTTGGTGAAG AAGTTGAAAT</u> | | | | 154 |

| | | |
|---------------------------------|---|-----|
| Gardnerella vaginalis | CACGATCTTG <u>ACAAGCCATT</u> CTTGATGCCA ATCGA...CGTGG TAAGCTCCCA ATCAACACCC CAGTTGAGAT | 135 |
| Haemophilus influenzae | CGTGCGATTG <u>ACCAACGGTT</u> CCTTCCTCCA ATCGA...CGAGG TATTATCCGT ACAGGTGATG AAGTAGAAAT | 157 |
| 5 Helicobacter pylori | AGAGACACTG <u>AAAAAAGTTT</u> CTTGATGCCG GTTGA...AGAGG CGTGGTGAAA GTAGGCGATG AAGTGGAAAT | 158 |
| Listeria monocytogenes | CGTGATACTG <u>ACAAACCATT</u> CATGATGCCA GTTGA...CGTGG ACAAGTTAAA GTTGGTGACG AAGTAGAAGT | 138 |
| Micrococcus luteus | CGCGACAAGG <u>ACAAGCCGTT</u> CCTGATGCCG ATCGA...CGCGG CACCCTGAAG ATCAACTCCG AGGTCGAGAT | 159 |
| Mycobacterium tuberculosis | CGCGAGACCG <u>ACAAGCCGTT</u> CCTGATGCCG GTCGA...CGCGG CGTGATCAAC GTGAACGAGG AAGTTGAGAT | 160 |
| Mycoplasma genitalium | CGTGAAGTAG <u>ATAAACCTTT</u> CTTATAGCA ATTGA...AGAGG TGAATCAAA GTAGGTCAAG AAGTTGAAAT | 161 |
| 15 Neisseria gonorrhoeae | CGTGCCGTGG <u>ACAAACCATT</u> CCTGCTGCCT ATCGA...CGAGG TATCATCCAC GTTGGTGACG AGATTGAAAT | 162 |
| Salmonella typhimurium | CGTGCGATTG <u>ACAAGCCGTT</u> CCTGCTGCCG ATCGA...CGCGG TATCATCAAA GTGGCGAAG AAGTTGAAAT | 164 |
| Shewanella putida | CGTGACATCG <u>ATAAGCCGTT</u> CCTACTGCCA ATCGA...CGTGG TATTGTACGC GTAGGCGACG AAGTTGAAAT | 165 |
| Staphylococcus aureus | CGTGATTTCTG <u>ACAAACCATT</u> CATGATGCCA GTTGA...CGTGG TCAAAATCAA GTTGGTGAAG AAGTTGAAAT | 140 |
| Staphylococcus epidermidis | CGTGATTTCTG <u>ACAAACCATT</u> CATGATGCCA GTTGA...CGTGG TCAAAATCAA GTWGGTGAAG AAGTTGAAAT | 141 |
| 25 Staphylococcus saprophyticus | CGTGATTTCTG <u>ACAAACCATT</u> CATGATGCCA GTTGA...CGTGG TCAAAATCAA GTGGGTGAAG AAATCGARAT | 142 |

Streptococcus 144
agalactiae
Streptococcus 145
pneumoniae
5 Streptococcus 167
pyogenes
Ureaplasma 170
urealyticum
Selected
10 sequences

SEQ ID NO: 14*

SEQ ID NO: 13

Selected
genus-specific
primer
15 sequences:

The sequence numbering refers to the *E. faecalis* *tuf* gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

20 * This sequence is the reverse complement of the above *tuf* sequence.

NOTE: The above primers also amplify *tuf* sequences from *Abiotrophia* species; this genus has recently been related to the *Enterococcus* genus by 16S rRNA analysis.

Annex III: Strategy for the selection from *tuf* sequences of the amplification primers specific for the genus *Staphylococcus* (continues on pages 56 and 57).

| | 385 | 420.....579 | 611 SEQ ID NO |
|-----------------------------------|------------|---|---------------|
| 5 <i>Bacillus subtilis</i> | TGGCCGTGTA | GAACGCGGAC AAGTTAAAGT CGG.....TTG CTAAACCCAGG TACAATCACT CCACACAGCA | 148 |
| <i>Bacteroides fragilis</i> | AGGTCGTATC | GAAACTGGTG TTAATCATGT AGG.....TTT GTAAACCCGGG TCAGATTAAA CCTCACTCTA | 149 |
| <i>Burkholderia cepacia</i> | GGGTCGTGTC | GAGCGCGGCA TCGTGAAAGT CGG.....TGG CGAAGCCGGG TTGGATCAGG CCGCACACGC | 152 |
| <i>Chlamydia trachomatis</i> | TGGACGTAAT | GAGCGTGGAA TTGTTAAAGT TTC.....TTT GCTTGCCAAA CAGTGTTAAA CCTCATACAC | 153 |
| <i>Corynebacterium diptheriae</i> | CGGCCGTGTT | GAGCGTGGCT CCCTGAAGT CAA.....TTG TTAAGCCAGG CGCTTACACC CCTCACACCG | 126 |
| 15 <i>Enterococcus faecalis</i> | AGGACGTGTT | GAACGTGGTG AAGTTCGCGT TGG.....TAG CTAAACCCAGC TACAATCACT CCACACACAA | 132 |
| <i>Enterococcus faecium</i> | AGGTCGTGTT | GAACGTGGAC AAGTTCGCGT TGG.....TAG CTAAACCCAGG TACAATCACT CCTCTACAA | 133 |
| <i>Escherichia coli</i> | CGGTCGTGTA | GAACGCGGTA TCATCAAAGT TGG.....TGG CTAAGCCGGG CACCATCAAG CCGCACACCA | 154 |
| 20 <i>Gardnerella vaginalis</i> | CGGTCGTGTT | GAGCGTGGTA AGCTCCCAAT CAA.....TGG CTGCTCCAGG TTCTGTGACT CCACACACCA | 135 |

- 55 -

| | | |
|-------------------------------------|---|-----|
| <i>Haemophilus influenzae</i> | AGGTCGTGTA <u>GAACGAGGTA</u> TTATCCGTAC AGG.....TAG CGAAACCCAGG TTCAATCACA CCACACACTG | 157 |
| <i>Helicobacter pylori</i> | AGGTAGGATT <u>GAAAGAGCG</u> TGGTGAAGT AGG.....TAT GCAAACCCAGG TTCTATCACT CCGCACACAGA | 158 |
| 5 <i>Listeria monocytogenes</i> | TGGACGTGTT <u>GAACGTGGAC</u> AAGTTAAAGT TGG.....TAG CTAAACCCAGG TTGGATTACT CCACACACTA | 138 |
| <i>Micrococcus luteus</i> | CGGTCGCGCC <u>GAGCGCGCA</u> CCCTGAAGAT CAA.....TGG TGGAGCCGGG CTCCATCACC CCGCACACCA | 159 |
| <i>Mycobacterium tuberculosis</i> | CGGACGTGTG <u>GAGCGCGCG</u> TGATCAAGT GAA.....TCA CCAAGCCGGG CACCACCCAG CCGCACACCG | 160 |
| <i>Mycoplasma genitalium</i> | AGGAAGAGTT <u>GAAAGAGGTG</u> AACTCAAGT AGG.....TAG CAAAACCCAGG CTCTATTAAA CCGCACACAGA | 161 |
| <i>Neisseria gonorrhoeae</i> | CGGCCGTGTA <u>GAGCGAGGTA</u> TCATCCAGT TGG.....TGG CCAAACCCGGG TACTATCACT CCTCACACCA | 162 |
| 15 <i>Salmonella typhimurium</i> | CGGTCGTGTA <u>GAGCGCGGTA</u> TCATCAAGT GGG.....TGG CTAAGCCGGG CACCATCAAG CCGCACACCA | 164 |
| <i>Shewanella putida</i> | AGGTCGTGTT <u>GAGCGTGTA</u> TTGTACCGT AGG.....TAG CGAAGCCAGG TTCAATCAAC CCACACACTA | 165 |
| <i>Staphylococcus aureus</i> | AGGCCGTGTT <u>GAACGTGGTC</u> AAATCAAGT TGG.....TAG CTGCTCCTGG TTCAATTACA CCACATACTG | 140 |
| <i>Staphylococcus epidermidis</i> | AGGCCGTGTT <u>GAACGTGGTC</u> AAATCAAGT WGG.....TAG CTGCTCCTGG TTCTATTACA CCACACACAA | 141 |
| <i>Staphylococcus saprophyticus</i> | AGGCCGTGTT <u>GAACGTGGTC</u> AAATCAAGT CGG.....TAG CTGCTCCTGG TACTATCACA CCACATACAA | 142 |
| 25 <i>Staphylococcus simulans</i> | AGGCCGTGTT <u>GAACGTGGTC</u> AAATCAAGT CGG.....TAG CAGCTCCTGG CTCTATTACT CCACACACAA | 143 |

Streptococcus
agalactiae
Streptococcus
pneumoniae
5 Ureaplasma
urealyticum
Selected
sequences^a

AGGACGTATC GACCGTGGTA CTGTTCTGTGT CAA.....TTG CTAAACCAGG TTCAATCAAC CCACACACTA 144
AGGACGTATC GACCGTGGTA TCGTTAAAGT CAA.....TCG CTAAACCAGG TTCAATCAAC CCACACACTA 145
TGGACGTGTT GAACGTGGTG TATTAAAGT TAA.....TTG TAAACCAGG ATCAATTAAA CCTCACCCTA 170
CCGTGTT GAACGTGGTC AAATCAAA GCTCCTGG YMCWATYACA CCACAYA

SEQ ID NO: 18^b

SEQ ID NO: 17

10 Selected
genus-specific
primer
sequences^a:

TRTGTGGT GTRATWGWRC CAGGAGC

CCGTGTT GAACGTGGTC AAATCAAA

15 The sequence numbering refers to the *S.aureus* tuf gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

^a "R", "W" and "Y" designate nucleotide positions which are degenerated. "R" stands for A or G; "W", for A or T; "Y", for C or T.

20 ^b This sequence is the reverse complement of the above tuf sequence.

Annex IV: Strategy for the selection from *tuf* sequences of the amplification primers specific for the species *Candida albicans* (continues on pages 59 and 60).

| | 58 | 90 | 181 | 213 SEQ ID NO |
|-----------------------------------|---|----|-----|---------------|
| <i>Candida albicans</i> | CGTCAAGAAG GTTGGTTACA ACCCAAGAC TGT...CAA ATCCGGTAAA GTTACTGGTA AGACCTTGTT | | | 120 |
| <i>Candida glabrata</i> | CATCAAGAAG GTCGGTTACA ACCCAAGAC TGT...CAA GGCTGGTGTC GTCAAGGGTA AGAYCTTGTT | | | 121 |
| <i>Candida krusei</i> | CATCAAGAAG GTTGGTTACA ACCCAAGAC TGT...CAA GGCAGGTGTT GTTAAGGGTA AGACCTTATT | | | 122 |
| <i>Candida parapsilosis</i> | CGTCAAGAAG GTTGGTTACA ACCCTAAGC TGT...TAA AGCTGGTAAG GTTACCGGTA AGACCTTGTT | | | 123 |
| <i>Candida tropicalis</i> | CGTCAAGAAG GTTGGTTACA ACCCTAAGC TGT...CAA GGCTGGTAAG GTTACCGGTA AGACTTGT | | | 124 |
| <i>Schizo-saccharomyces pombe</i> | CATCAAGAAG GTCGGTTTCA ACCCAAGAC CGT...CAA GGCTGGTGTC GTCAAGGGTA AGACTCTTTT | | | |
| Human | GGAGATCCGG GAGCTGCTCA CCGAGTTGG CTA...GTT AGGCTGTAAG TCTGTGCAGA AGCTACTGGA | | | |
| 15 <i>Chlamydia trachomatis</i> | GGAGCTCGC GAGCTGCTCA GCAAGTACG CTT...CAA ATG..... ..TATCTGG AGCTGATGAA | | | 153 |
| <i>Corynebacterium diptheriae</i> | GGAGATCCRT GAGCTGCTCG CTGAGCAGGA TTA...GAA GTGGACCCAG TCCATCATCG ACCTCATGCA | | | 126 |
| <i>Enterococcus faecalis</i> | GGAGTTCTGT GACTTATTAT CAGATACGA TTT..... ..TGAAGA AAAATCTTAG AATTAATGGC | | | 132 |
| 20 <i>Escherichia coli</i> | GGAGTTCTGT GAAGTTCTGT CTCAGTACGA CTT..... ..GGGAAGCG AAAATCTTGG AACTGGCTGG | | | 154 |

| | | | | | | | | |
|-------------------|-------------|-------------|------------|-----------|------------|------------|------------|-----|
| Flavobacterium | CGAGGTTCCG | GAAAGAACTGA | CTAAACGCCG | TTT..... | ..GGGTAAA | GAAATGAAA | ACCTGATGGA | 156 |
| ferrugineum | | | | | | | | |
| Gardnerella | AGAGGTCCGT | GACCTCCTCG | AAGAAAACCG | CTT...CAA | GTGGGTAGAG | ACCGTCAAGG | AATCATGAA | 135 |
| vaginalis | | | | | | | | |
| 5 Haemophilus | GGAAAGTTCCG | GAACTTCTAT | CTCAATATGA | CTT..... | ..GGGAAGAA | AAATCCTTG | AGTTAGCAAA | 157 |
| influenzae | | | | | | | | |
| Listeria | GGAAATTCGT | GATCTATTAA | CTGAATATGA | ATT..... | ..GGGAAGCT | AAATTGACG | AGTTAATGGA | 138 |
| monocytogenes | | | | | | | | |
| Micrococcus | GGAAAGTCCGT | GAGTTGCTGG | CTGCCCAGGA | ATT...CAA | GIGGCTCGAG | TCGTGCACAC | AGTTGATGGA | 159 |
| 10 luteus | | | | | | | | |
| Neisseria | GGAAATCCGC | GACCTGCTGT | CCAGCTACGA | CTT..... | ..ACGAAGAA | AAATCTTCG | AACTGGCTAC | 162 |
| gonorrhoeae | | | | | | | | |
| Salmonella | GGAAAGTTCCG | GAACTGCTGT | CTCAGTACGA | CTT..... | ..GGGAAGCG | AAATCATCG | AACTGGCTGG | 164 |
| typhimurium | | | | | | | | |
| 15 Staphylococcus | GGAAAGTTCCG | GACTTATTAA | GCGAATATGA | CTT..... | ...CGAAGAA | AAATCTTAG | AATTAATGGA | 140 |
| aureus | | | | | | | | |
| Streptococcus | GGAAATCCGT | GACCTATTGT | CAGAATACGA | CTT..... | ...CGAAGAC | ATCGTTATGG | AATTGATGAA | 145 |
| pneumoniae | | | | | | | | |
| Treponema | AGAGGTCCGT | GATGCGCTTG | CTGGATATGG | GTT...GGA | GGATGCAGCT | TGTATTGAGG | AACTGCTTGC | 169 |
| 20 pallidum | | | | | | | | |

- 60 -

| | | |
|--|-------------------------------------|-------------------------------------|
| Selected sequences | <u>CAAGAAG GTTGTTTACA ACCCAAAGA</u> | <u>ATCCGGTAAA GTTACTGGTA AGACCT</u> |
| Selected | SEQ ID NO: 11 | SEQ ID NO: 12* |
| 5 species-specific primer sequences: | CAAGAAG GTTGTTTACA ACCCAAAGA | AGGTCCTACC AGTAACTTTAC CGGAT |

10 The sequence numbering refers to the *Candida albicans* *tuf* gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

* This sequence is the reverse-complement of the above *tuf* sequence.

Annex V: Strategy for the selection from the *recA* gene of the amplification primers specific for the genus *Streptococcus* (continues on pages 62 and 63).

| | 415 | 449...540 | 574 SEQ ID NO |
|--|------------|---|------------------|
| 5 <i>Bordetella pertussis</i> | CTCGAGATCA | CCGACGGCT GGTGGCTCG GGCTC...GGCCC GCTGATGAG CCAGGGCGTG CGCAAGCTGA | |
| <i>Burkholderia cepacia</i> | CTCGAATCA | CCGATGGCT GGTGGCTCG GGCTC...GGCCC GCTGATGTC GCAGGGCGTG CGCAAGCTGA | |
| <i>Campylobacter jejuni</i> | TTAGAAATTG | TAGAACTAT AGCAAGAAGT GGCG...AGCAA GACTTATGTC TCAAGCTCTA AGAAACTTA | |
| <i>Chlamydia trachomatis</i> | TTGAGTATTG | CAGAGCTCTT AGCGGTTCT GGAG...AGCTC GCATGATGTC GCAGGCTCTA CGCAATTA | |
| <i>Clostridium perfringens</i> | TTAGAAATAA | CAGAAGCTTT AGTTAGATCA GGAG...AGCTA GATTAATGTC ACAAGCTTA AGAAAGTTAA | |
| 15 <i>Corynebacterium pseudotuberculosis</i> | CTCGAGATTG | CAGATATGCT TGTTCGCTCT GGAG...AGCGC GTTGTATGAG TCAGGGCGTG CGTAAGATGA | |
| <i>Enterobacter agglomerans</i> | CTGGAATCT | GTGATGGCT GACCGTTCA GGCG...AGCTC GTATGATGAG CCAGGGCGTG CGTAAGCTTG | |
| <i>Enterococcus faecium</i> | TTAGAGATTG | CCGATGCCCTT AGTTCAAGT GGTC...AGCTC GACTAATGTC TCAAGCACTA CGTAAATTAT | |
| 20 <i>Escherichia coli</i> | CTGGAATCT | GTGAGCCCTT GGCGGTTCT GGCG...GGCAC GTATGATGAG CCAGGGCGTG CGTAAGCTGG | |

| | | |
|------------------|---|----|
| Haemophilus | CGGAACAGAA GAATAGAAAT TTAATGCATT ACCGC...GACCT GTGAGTTTAC GCAAGCTTG AGACATTAAA | |
| influenzae | | |
| Helicobacter | TTAGAAATTT TAGAAACGAT CACCAGAGC GGAGG...AGCAA GGCTATGAG CCATCGGTTA AGAAAAATCA | |
| pylori | | |
| 5 Lactococcus | CTTCAAATTG CTGAATAATT GATTACTTCT GGAGC...AGCAC GTATGATGTC ACAAGCCATG CGTAAACTTG | |
| lactis | | |
| Legionella | CTGGAAATTA CTGATATGCT GGTCGGTTCT GCAGC...GGCAA GATTGATGTC GCAAGCCCTG CGTAAATTGA | |
| pneumophila | | |
| Mycoplasma | TTTGCTCTTA TCGAATCATT AATTAAACA AACAA...TGCAA GAATGATGTC AAAAGGTTTG CGAAGRATAC | |
| 10 genitalium | | |
| Neisseria | TTGGAAATCT GCGACACGCT CGTCCGTTCT GGCGG...GGCGC GCCTGATGAG TCAGGCTTTG CGCAAACTGA | |
| gonorrhoeae | | |
| Proteus | CTGGAATTT GTGATGCATT ATCTCGCTCT GGTGC...CGCAC GTATGATGAG CCAAGCTATG CGTAAACTAG | |
| mirabilis | | |
| 15 Pseudomonas | CTGGAAATCA CCGACATGCT GGTCGGCTCC AACGC...GGCAC GCCTGATGTC CCAGGCGCTG CGCAAGATCA | |
| aeruginosa | | |
| Serratia | CTGGAATCT GTGATGCGCT GACCCGCTCC GGCGC...GGCGC GCATGATGAG CCAGGCGATG CGTAACTGG | |
| marcescens | | |
| Shigella | CTGGAAATCT GTGACGCCCT GGCGCGTTCT GGCGC...GGCAC GTATGATGAG CCAGGCGATG CGTAACTGG | |
| 20 flexneri | | |
| Staphylococcus | CTTGAATCG CCGAAGCATT TGTTAGAACT GGTGC...AGCTC GTTTAATGTC ACAAGCGTTA CGTAAACTTT | |
| aureus | | |
| Streptococcus | TTAGAAATTG CAGGAATAAT GATTGACTCT GGGGC..... | 32 |
| gordonii | | |
| 25 Streptococcus | CTTGAATTG CAGGGAATT GATTGATTCT GGCGC...AGCAC GCATGATGAG TCAAGCGATG CGTAAATTAT | 33 |
| mutans | | |

Streptococcus 34
pneumoniae CTTGAGATTG CCGGAAAATT GATTGACTCA GGTGC...GGCTC GTATGATGAG CCAGGCCATG CGTAAACTTG
Streptococcus 35
pyogenes CTTGAAATTG CAGGAAAATT GATTGATTCT GGTGC...AGCAC GTATGATGAG TCAGGCCATG CGTAAATTAT
5 Streptococcus 36
salivarius CTCGAAATTG CAGGTAAGCT GATTGACTCT GGTGC...AGCGC GTATGATGAG TCAAGCCATG CGTAAACTTT
Vibrio CTGGAATTG GTGATGCACT GGTGC...AGCGC GTATGATGAG TCAAGCCATG CGTAAACTTG
cholerae CTGGAATTG GTGATGCACT GGTGC...AGCGC GTATGATGAG TCAAGCCATG CGTAAACTTG
Yersinia CTGGAATTG GTGATGCACT GGTGC...AGCGC GTATGATGAG TCAAGCCATG CGTAAACTTG
10 pestis CTGGAATTG GTGATGCACT GGTGC...AGCGC GTATGATGAG TCAAGCCATG CGTAAACTTG
Selected GAAATTG CAGGAAAATT GATTGA ATGATGAG TCAAGCCATG CGTAA
sequences*
Selected SEQ ID NO: 21 SEQ ID NO: 22^b
15 genus-specific GAAATTG CAGGAAAATT GATTGA TTACGCAT GGCITGACTC ATCAT
primer
sequences*:

The sequence numbering refers to the *S.pneumoniae* recA sequence. Underlined nucleotides are identical to the selected sequence or match that sequence.

^a "I" stands for inosine which is a nucleotide analog that can bind to any of the four nucleotides A, C, G or T.
^b This sequence is the reverse complement of the above recA sequence.

Annex VI: Specific and ubiquitous primers for DNA amplification

| | SEQ ID NO | Nucleotide sequence | Originating DNA fragment | |
|----|---|---|--------------------------|---------------------|
| | | | SEQ ID NO | Nucleotide position |
| 5 | <u>Bacterial species:</u> <i>Enterococcus faecium</i> | | | |
| | 1 | 5'-TGC TTT AGC AAC AGC CTA TCA G | 26 ^a | 273-294 |
| | 2 ^b | 5'-TAA ACT TCT TCC GGC ACT TCG | 26 ^a | 468-488 |
| 10 | <u>Bacterial species:</u> <i>Listeria monocytogenes</i> | | | |
| | 3 | 5'-TGC GGC TAT AAA TGA AGA GGC | 27 ^a | 339-359 |
| | 4 ^b | 5'-ATC CGA TGA TGC TAT GGC TTT | 27 ^a | 448-468 |
| 15 | <u>Bacterial species:</u> <i>Neisseria meningitidis</i> | | | |
| | 5 | 5'-CCA GCG GTA TTG TTT GGT GGT | 28 ^a | 56-76 |
| | 6 ^b | 5'-CAG GCG GCC TTT AAT AAT TTC | 28 ^a | 212-232 |
| 20 | <u>Bacterial species:</u> <i>Staphylococcus saprophyticus</i> | | | |
| | 7 | 5'- AGA TCG AAT TCC ACA TGA AGG TTA TTA TGA | 29 ^c | 290-319 |
| | 8 ^b | 5'- TCG CTT CTC CCT CAA CAA TCA AAC TAT CCT | 29 ^c | 409-438 |
| 25 | <u>Bacterial species:</u> <i>Streptococcus agalactiae</i> | | | |
| | 9 | 5'-TTT CAC CAG CTG TAT TAG AAG TA | 30 ^a | 59-81 |
| | 10 ^b | 5'-GTT CCC TGA ACA TTA TCT TTG AT | 30 ^a | 190-212 |
| 30 | <u>Fungal species:</u> <i>Candida albicans</i> | | | |
| | 11 | 5'-CAA GAA GGT TGG TTA CAA CCC AAA GA | 120 ^c | 61-86 |
| | 12 ^b | 5'-AGG TCT TAC CAG TAA CTT TAC CGG AT | 120 ^c | 184-209 |

^a Sequences from databases.

35 ^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

^c Sequences determined by our group.

Annex VI: Specific and ubiquitous primers for DNA amplification
(continues on next page)

| | SEQ ID NO | Nucleotide sequence | Originating DNA fragment | |
|----|--|--------------------------------------|--|----------------------|
| | | | SEQ ID NO | Nucleotide position |
| 5 | <u>Bacterial genus: Enterococcus</u> | | | |
| | 13 | 5'-TAC TGA CAA ACC ATT CAT GAT G | 131-134 ^{a,b} | 319-340 ^c |
| | 14 ^d | 5'-AAC TTC GTC ACC AAC GCG AAC | 131-134 ^{a,b} | 410-430 ^c |
| | <u>Bacterial genus: Neisseria</u> | | | |
| 10 | 15 | 5'-CTG GCG CGG TAT GGT CGG TT | 31 ^e | 21-40 ^f |
| | 16 ^d | 5'-GCC GAC GTT GGA AGT GGT AAA G | 31 ^e | 102-123 ^f |
| | <u>Bacterial genus: Staphylococcus</u> | | | |
| 15 | 17 | 5'-CCG TGT TGA ACG TGG TCA AAT CAA A | 140-143 ^{a,b} | 391-415 ^g |
| | 18 ^d | 5'-TRT GTG GTG TRA TWG WRC CAG GAG C | 140-143 ^{a,b} | 584-608 ^g |
| | 19 | 5'-ACA ACG TGG WCA AGT WTT AGC WGC T | 140-143 ^{a,b} | 562-583 ^g |
| | 20 ^d | 5'-ACC ATT TCW GTA CCT TCT GGT AAG T | 140-143 ^{a,b} | 729-753 ^g |
| 20 | <u>Bacterial genus: Streptococcus</u> | | | |
| | 21 | 5'-GAA ATT GCA GGI AAA TTG ATT GA | 32-36 ^e | 418-440 ^h |
| | 22 ^d | 5'-TTA CGC ATG GCI TGA CTC ATC AT | 32-36 ^e | 547-569 ^h |
| 25 | <u>Universal primers</u> | | | |
| | 23 | 5'-ACI KKI ACI GGI GTI GAR ARG TT | 118-146 ^{a,b} 147-171 ^{a,e} | 493-515 ⁱ |
| | 24 ^d | 5'-AYR TTI TCI CCI GGC ATI ACC AT | 118-146 ^{a,b} 147-171 ^{a,e} | 778-800 ⁱ |

- 30 ^a These sequences were aligned to derive the corresponding primer.
- ^b *tuf* sequences determined by our group.
- ^c The nucleotide positions refer to the *E. faecalis tuf* gene fragment (SEQ ID NO: 132).
- 35 ^d These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.
- ^e Sequences from databases.
- ^f The nucleotide positions refer to the *N. meningitidis asd* gene fragment (SEQ ID NO: 31).

- ⁹ The nucleotide positions refer to the *S. aureus* *tuf* gene fragment (SEQ ID NO: 140).
- ^h The nucleotide positions refer to the *S. pneumoniae* *recA* gene (SEQ ID NO: 34).
- 5 ⁱ The nucleotide positions refer to the *E. coli* *tuf* gene fragment (SEQ ID NO: 154).

Annex VI: Specific and ubiquitous primers for DNA amplification

| SEQ ID NO | Nucleotide sequence | Originating DNA fragment | |
|--|--|--------------------------|---------------------|
| | | SEQ ID NO | Nucleotide position |
| <u>Antibiotic resistance gene: bla_{tem}</u> | | | |
| 5 | 37 5'-CTA TGT GGC GCG GTA TTA TC | - | - |
| | 38 5'-CGC AGT GTT ATC ACT CAT GG | - | - |
| 10 | 39 5'-CTG AAT GAA GCC ATA CCA AA | - | - |
| | 40 5'-ATC AGC AAT AAA CCA GCC AG | - | - |
| <u>Antibiotic resistance gene: bla_{shv}</u> | | | |
| 15 | 41 5'-TTA CCA TGA GCG ATA ACA GC | - | - |
| | 42 5'-CTC ATT CAG TTC CGT TTC CC | - | - |
| 20 | 43 5'-CAG CTG CTG CAG TGG ATG GT | - | - |
| | 44 5'-CGC TCT GCT TTG TTA TTC GG | - | - |
| <u>Antibiotic resistance gene: bla_{rob}</u> | | | |
| 25 | 45 5'-TAC GCC AAC ATC GTG GAA AG | - | - |
| | 46 5'-TTG AAT TTG GCT TCT TCG GT | - | - |
| 30 | 47 5'-GGG ATA CAG AAA CGG GAC AT | - | - |
| | 48 5'-TAA ATC TTT TTC AGG CAG CG | - | - |
| <u>Antibiotic resistance gene: bla_{oxa}</u> | | | |
| 35 | 49 5'-GAT GGT TTG AAG GGT TTA TTA TAA G | 110 ^a | 686-710 |
| | 50 ^b 5'-AAT TTA GTG TGT TTA GAA TGG TGA T | 110 ^a | 802-826 |
| <u>Antibiotic resistance gene: bla_Z</u> | | | |
| 40 | 51 5'-ACT TCA ACA CCT GCT GCT TTC | 111 ^a | 511-531 |
| | 52 ^b 5'-TGA CCA CTT TTA TCA GCA ACC | 111 ^a | 663-683 |
| <u>Antibiotic resistance gene: aadB</u> | | | |
| 45 | 53 5'-GGC AAT AGT TGA AAT GCT CG | - | - |
| | 54 5'-CAG CTG TTA CAA CGG ACT GG | - | - |
| <u>Antibiotic resistance gene: aacC1</u> | | | |
| 50 | 55 5'-TCT ATG ATC TCG CAG TCT CC | - | - |
| | 56 5'-ATC GTC ACC GTA ATC TGC TT | - | - |

^a Sequences from databases.^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

Annex VI: Specific and ubiquitous primers for DNA amplification

| | SEQ ID NO | Nucleotide sequence | Originating DNA fragment | | |
|----|--|--------------------------------|--------------------------|---------------------|--|
| | | | SEQ ID NO | Nucleotide position | |
| 5 | <u>Antibiotic resistance gene: aacC2</u> | | | | |
| | 57 | 5'-CAT TCT CGA TTG CTT TGC TA | - | - | |
| | 58 | 5'-CCG AAA TGC TTC TCA AGA TA | - | - | |
| 10 | <u>Antibiotic resistance gene: aacC3</u> | | | | |
| | 59 | 5'-CTG GAT TAT GGC TAC GGA GT | - | - | |
| | 60 | 5'-AGC AGT GTG ATG GTA TCC AG | - | - | |
| 15 | <u>Antibiotic resistance gene: aac6'-IIa</u> | | | | |
| | 61 | 5'-GAC TCT TGA TGA AGT GCT GG | 112 ^a | 123-142 | |
| | 62 ^b | 5'-CTG GTC TAT TCC TCG CAC TC | 112 ^a | 284-303 | |
| 20 | 63 | 5'-TAT GAG AAG GCA GGA TTC GT | 112 ^a | 445-464 | |
| | 64 ^b | 5'-GCT TTC TCT CGA AGG CTT GT | 112 ^a | 522-541 | |
| | <u>Antibiotic resistance gene: aacA4</u> | | | | |
| 25 | 65 | 5'-GAG TTG CTG TTC AAT GAT CC | - | - | |
| | 66 | 5'-GTG TTT GAA CCA TGT ACA CG | - | - | |
| | <u>Antibiotic resistance gene: aad(6')</u> | | | | |
| 30 | 173 | 5'-TCT TTA GCA GAA CAG GAT GAA | - | - | |
| | 174 | 5'-GAA TAA TTC ATA TCC TCC G | - | - | |
| | <u>Antibiotic resistance gene: vanA</u> | | | | |
| 35 | 67 | 5'-TGT AGA GGT CTA GCC CGT GT | - | - | |
| | 68 | 5'-ACG GGG ATA ACG ACT GTA TG | - | - | |
| | 69 | 5'-ATA AAG ATG ATA GGC CGG TG | - | - | |
| | 70 | 5'-TGC TGT CAT ATT GTC TTG CC | - | - | |
| 40 | <u>Antibiotic resistance gene: vanB</u> | | | | |
| | 71 | 5'-ATT ATC TTC GGC GGT TGC TC | 116 ^a | 22-41 | |
| | 72 ^b | 5'-GAC TAT CGG CTT CCC ATT CC | 116 ^a | 171-190 | |
| 45 | 73 | 5'-CGA TAG AAG CAG CAG GAC AA | 116 ^a | 575-594 | |
| | 74 ^b | 5'-CTG ATG GAT GCG GAA GAT AC | 116 ^a | 713-732 | |

^a Sequences from databases.^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

Annex VI: Specific and ubiquitous primers for DNA amplification

| | SEQ ID NO | Nucleotide sequence | Originating DNA fragment | |
|----|--|-----------------------------------|--------------------------|---------------------|
| | | | SEQ ID NO | Nucleotide position |
| 5 | <u>Antibiotic resistance gene: <i>vanC</i></u> | | | |
| | 75 | 5'-GCC TTA TGT ATG AAC AAA TGG | 117 ^a | 373-393 |
| | 76 ^b | 5'-GTG ACT TTW GTG ATC CCT TTT GA | 117 ^a | 541-563 |
| 10 | <u>Antibiotic resistance gene: <i>msrA</i></u> | | | |
| | 77 | 5'-TCC AAT CAT TGC ACA AAA TC | - | - |
| | 78 | 5'-AAT TCC CTC TAT TTG GTG GT | - | - |
| 15 | 79 | 5'-TCC CAA GCC AGT AAA GCT AA | - | - |
| | 80 | 5'-TGG TTT TTC AAC TTC TTC CA | - | - |
| 20 | <u>Antibiotic resistance gene: <i>sata</i></u> | | | |
| | 81 | 5'-TCA TAG AAT GGA TGG CTC AA | - | - |
| | 82 | 5'-AGC TAC TAT TGC ACC ATC CC | - | - |
| 25 | <u>Antibiotic resistance gene: <i>aac(6')-aph(2'')</i></u> | | | |
| | 83 | 5'-CAA TAA GGG CAT ACC AAA AAT C | - | - |
| | 84 | 5'-CCT TAA CAT TTG TGG CAT TAT C | - | - |
| | 85 | 5'-TTG GGA AGA TGA AGT TTT TAG A | - | - |
| | 86 | 5'-CCT TTA CTC CAA TAA TTT GGC T | - | - |
| 30 | <u>Antibiotic resistance gene: <i>vat</i></u> | | | |
| | 87 | 5'-TTT CAT CTA TTC AGG ATG GG | - | - |
| | 88 | 5'-GGA GCA ACA TTC TTT GTG AC | - | - |
| 35 | <u>Antibiotic resistance gene: <i>vga</i></u> | | | |
| | 89 | 5'-TGT GCC TGA AGA AGG TAT TG | - | - |
| | 90 | 5'-CGT GTT ACT TCA CCA CCA CT | - | - |
| 40 | <u>Antibiotic resistance gene: <i>ermA</i></u> | | | |
| | 91 | 5'-TAT CTT ATC GTT GAG AAG GGA TT | 113 ^a | 370-392 |
| | 92 ^b | 5'-CTA CAC TTG GCT TAG GAT GAA A | 113 ^a | 487-508 |

45 ^a Sequences from databases.

^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

Annex VI: Specific and ubiquitous primers for DNA amplification

| | SEQ ID NO | Nucleotide sequence | Originating DNA fragment | |
|----|--|--|--------------------------|---------------------|
| | | | SEQ ID NO | Nucleotide position |
| | <u>Antibiotic resistance gene: <i>ermB</i></u> | | | |
| 5 | 93 | 5'-CTA TCT GAT TGT TGA AGA AGG ATT | 114 ^a | 366-389 |
| | 94 ^b | 5'-GTT TAC TCT TGG TTT AGG ATG AAA | 114 ^a | 484-507 |
| | <u>Antibiotic resistance gene: <i>ermC</i></u> | | | |
| 10 | 95 | 5'-CTT GTT GAT CAC GAT AAT TTC C | 115 ^a | 214-235 |
| | 96 ^b | 5'-ATC TTT TAG CAA ACC CGT ATT C | 115 ^a | 382-403 |
| | <u>Antibiotic resistance gene: <i>mecA</i></u> | | | |
| 15 | 97 | 5'-AAC AGG TGA ATT ATT AGC ACT TGT AAG | - | - |
| | 98 | 5'-ATT GCT GTT AAT ATT TTT TGA GTT GAA | - | - |
| | <u>Antibiotic resistance gene: <i>int</i></u> | | | |
| 20 | 99 | 5'-GTG ATC GAA ATC CAG ATC C | - | - |
| | 100 | 5'-ATC CTC GGT TTT CTG GAA G | - | - |
| | 101 | 5'-CTG GTC ATA CAT GTG ATG G | - | - |
| 25 | 102 | 5'-GAT GTT ACC CGA GAG CTT G | - | - |
| | <u>Antibiotic resistance gene: <i>sul</i></u> | | | |
| | 103 | 5'-TTA AGC GTG CAT AAT AAG CC | - | - |
| 30 | 104 | 5'-TTG CGA TTA CTT CGC CAA CT | - | - |
| | 105 | 5'-TTT ACT AAG CTT GCC CCT TC | - | - |
| | 106 | 5'-AAA AGG CAG CAA TTA TGA GC | - | - |
| 35 | ^a Sequences from databases. | | | |
| | ^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing. | | | |

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

(A) NAME: INFECTIO DIAGNOSTIC (I.D.I.) INC.
(B) STREET: 2050, BOULEVARD RENE LEVESQUE OUEST, 4E ETAGE
(C) CITY: STE-FOY
(D) STATE: QUEBEC
(E) COUNTRY: CANADA
(F) POSTAL CODE (ZIP): G1V 2K8
(G) TELEPHONE: (418) 681-4343
(H) TELEFAX: (418) 681-5254

(A) NAME: BERGERON, MICHEL G.
(B) STREET: 2069 RUE BRULARD
(C) CITY: SILLERY
(D) STATE: QUEBEC
(E) COUNTRY: CANADA
(F) POSTAL CODE (ZIP): G1T 1G2

(A) NAME: PICARD, FRANCOIS J.
(B) STREET: 1245, RUE DE LA SAPINIERE
(C) CITY: CAP-ROUGE
(D) STATE: QUEBEC
(E) COUNTRY: CANADA
(F) POSTAL CODE (ZIP): G1Y 1A1

(A) NAME: OUELLETTE, MARC
(B) STREET: 1035 DE PLOERMEL
(C) CITY: SILLERY
(D) STATE: QUEBEC
(E) COUNTRY: CANADA
(F) POSTAL CODE (ZIP): G1S 3S1

(A) NAME: ROY, PAUL H.
(B) STREET: 28, RUE CHARLES GARNIER
(C) CITY: LORETTEVILLE
(D) STATE: QUEBEC
(E) COUNTRY: CANADA
(F) POSTAL CODE (ZIP): G2A 3S1

(ii) TITLE OF INVENTION: SPECIES-SPECIFIC, GENIUS-SPECIFIC AND
UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY
DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS
AND ASSOCIATED ANTIBIOTIC RESISTANCE GENES ...

(iii) NUMBER OF SEQUENCES: 174

(iv) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(vi) PRIOR APPLICATION DATA:

- 72 -

(A) APPLICATION NUMBER: US 08/743,637
(B) FILING DATE: 04-NOV-1996

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

TGCTTTAGCA ACAGCCTATC AG

22

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

TAAACTTCTT CCGGCACTTC G

21

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria monocytogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

TGCGGCTATA AATGAAGAGG C

21

(2) INFORMATION FOR SEQ ID NO: 4:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Listeria monocytogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

ATCCGATGAT GCTATGGCTT T

21

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria meningitidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CCAGCGGTAT TGTTTGGTGG T

21

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria meningitidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

CAGGCGGCCT TTAATAATTT C

21

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

AGATCGAATT CCACATGAAG GTTATTATGA

30

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

TCGCTTCTCC CTCAACAATC AACTATCCT

30

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Streptococcus agalactiae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

TTTCACCAGC TGTATTAGAA GTA

23

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Streptococcus agalactiae*

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

GTTCCCTGAA CATTATCTTT GAT

23

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Candida albicans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

CAAGAAGGTT GGTTACAACC CAAAGA

26

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Candida albicans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

AGGTCTTACC AGTAACTTTA CCGGAT

26

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

TACTGACAAA CCATTCATGA TG

22

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs

- 76 -

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

AACTTCGTCA CCAACGCGAA C

21

(2) INFORMATION FOR SEQ ID NO: 15:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

CTGGCGCGGT ATGGTCGGTT

20

(2) INFORMATION FOR SEQ ID NO: 16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

GCCGACGTTG GAAGTGGTAA AG

22

(2) INFORMATION FOR SEQ ID NO: 17:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

CCGTGTTGAA CGTGGTCAAA TCAA

25

(2) INFORMATION FOR SEQ ID NO: 18:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs

- 77 -

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

TRTGTGGTGT RATWGWCCA GGAGC

25

(2) INFORMATION FOR SEQ ID NO: 19:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

ACAACGTGGW CAAGTWTAG CWGCT

25

(2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

ACCATTTTCWG TACCTTCTGG TAAGT

25

(2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

GAAATTGCAG GNAAATTGAT TGA

23

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(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

TTACGCATGG CNTGACTCAT CAT

23

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:3
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:9
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:15
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

- 79 -

ACNKKNACNG GNGTNGARAT GTT

23

(2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:9
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:18
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

AYRTTNTCNC CNGGCATNAC CAT

23

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

TCGCTTCTCC

10

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 600 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

- 80 -

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

| | |
|---|-----|
| TTCTTAGAGA CATTGAATAT GCCTTATGTC GGCGCAGGCG TATTGACCAG TGCATGTGCC | 60 |
| ATGGATAAAA TCATGACCAA GTATATTTTA CAAGCTGCTG GTGTGCCGCA AGTTCCTTAT | 120 |
| GTACCACTAC TTAAGAATCA ATGGAAAGAA AATCCTAAAA AAGTATTTGA TCAATGTGAA | 180 |
| GGTTCTTTGC TTTATCCGAT GTTTGTCAAA CCTGCGAATA TGGGTTCTAG TGTCGGCATT | 240 |
| ACAAAGGCAG AAAACCGAGA AGAGCTGCAA AATGCTTTAG CAACAGCCTA TCAGTATGAT | 300 |
| TCTCGAGCAA TCGTTGAACA AGGAATTGAA GCGCGCGAAA TCGAAGTTGC TGTATTAGGA | 360 |
| AATGAAGATG TTCGGACGAC TTTGCCTGGC GAAGTCGTAA AAGACGTAGC ATTCTATGAT | 420 |
| TATGAAGCCA AATATATCAA TAATAAAATC GAAATGCAGA TTCCAGCCGA AGTGCCGGAA | 480 |
| GAAGTTTATC AAAAAGCGCA AGAGTACGCG AAGTTAGCTT ACACGATGTT AGGTGGAAGC | 540 |
| GGATTGAGCC GGTGCGATTT CTTTTTGACA AATAAAAATG AATTATTCCT GAATGAATTA | 600 |

(2). INFORMATION FOR SEQ ID NO: 27:

(i). SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1920 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria monocytogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

| | |
|---|-----|
| GTGGGATTAA ACAGATTAT GCGTGCGATG ATGGTGGTTT TCATTACTGC CAATTGCATT | 60 |
| ACGATTAACC CCGACATAAT ATTTGCAGCG ACAGATAGCG AAGATTCTAG TCTAAACACA | 120 |
| GATGAATGGG AAGAAGAAAA AACAGAAGAG CAACCAAGCG AGGTAAATAC GGGACCAAGA | 180 |
| TACGAACTG CACGTGAAGT AAGTTCACGT GATATTAAAG AACTAGAAAA ATCGAATAAA | 240 |
| GTGAGAAATA CGAACAAAGC AGACCTAATA GCAATGTTGA AAGAAAAAGC AGAAAAAGGT | 300 |
| CCAAATATCA ATAATAACAA CAGTGAACAA ACTGAGAATG CGGCTATAAA TGAAGAGGCT | 360 |

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| | |
|---|------|
| TCAGGAGCCG ACCGACCAGC TATACAAGTG GAGCGTCGTC ATCCAGGATT GCCATCGGAT | 420 |
| AGCGCAGCGG AAATTAAGAAA AAGAAGGAAA GCCATAGCAT CATCGGATAG TGAGCTTGAA | 480 |
| AGCCTTACTT ATCCGGATAA ACCAACAAAA GTAAATAAGA AAAAAGTGGC GAAAGAGTCA | 540 |
| GTTGCGGATG CTTCTGAAAG TGACTTAGAT TCTAGCATGC AGTCAGCAGA TGAGTCTTCA | 600 |
| CCACAACCTT TAAAAGCAAA CCAACAACCA TTTTCCCTA AAGTATTTAA AAAAATAAAA | 660 |
| GATGCGGGGA AATGGGTACG TGATAAAATC GACGAAAATC CTGAAGTAAA GAAAGCGATT | 720 |
| GTTGATAAAA GTGCAGGGTT AATTGACCAA TTATTAACCA AAAAGAAAAG TGAAGAGGTA | 780 |
| AATGCTTCGG ACTTCCCGCC ACCACCTACG GATGAAGAGT TAAGACTTGC TTTGCCAGAG | 840 |
| ACACCAATGC TTCTTGTTTT TAATGCTCCT GCTACATCAG AACCGAGCTC ATTCGAATTT | 900 |
| CCACCACCAC CTACGGATGA AGAGTTAAGA CTTGCTTTGC CAGAGACGCC AATGCTTCTT | 960 |
| GGTTTTAATG CTCCTGCTAC ATCGGAACCG AGCTCGTTTCG AATTTCACC GCCTCCAACA | 1020 |
| GAAGATGAAC TAGAAATCAT CCGGGAAACA GCATCCTCGC TAGATTCTAG TTTTACAAGA | 1080 |
| GGGGATTTAG CTAGTTTGAG AAATGCTATT AATCGCCATA GTCAAAATTT CTCTGATTTT | 1140 |
| CCACCAATCC CAACAGAAGA AGAGTTGAAC GGGAGAGGCG GTAGACCAAC ATCTGAAGAA | 1200 |
| TTTAGTTTCG TGAATAGTGG TGATTTTACA GATGACGAAA ACAGCGAGAC AACAGAAGAA | 1260 |
| GAAATTGATC GCCTAGCTGA TTTAAGAGAT AGAGGAACAG GAAAACACTC AAGAAATGCG | 1320 |
| GGTTTTTTTAC CATTAAATCC GTTTGCTAGC AGCCCGGTTT CTTTCGTTAAG TCCAAAGGTA | 1380 |
| TCGAAAATAA GCGACCGGGC TCTGATAAGT GACATAACTA AAAAAACGCC ATTTAAGAAT | 1440 |
| CCATCACAGC CATTAAATGT GTTTAATAAA AAAACTACAA CGAAAACAGT GACTAAAAAA | 1500 |
| CCAACCCCTG TAAAGACCGC ACCAAAGCTA GCAGAACTTC CTGCCACAAA ACCACAAGAA | 1560 |
| ACCGTACTTA GGGAAAATAA AACACCCCTT ATAGAAAAAC AAGCAGAAAC AAACAAGCAG | 1620 |
| TCAATTAATA TGCCGAGCCT ACCAGTAATC CAAAAAGAAG CTACAGAGAG CGATAAAGAG | 1680 |
| GAAATGAAAC CACAAACCGA GGAAAAAATG GTAGAGGAAA GCGAATCAGC TAATAACGCA | 1740 |
| AACGGAAAAA ATCGTTCTGC TGGCATTGAA GAAGGAAAAC TAATTGCTAA AAGTGCAGAA | 1800 |
| GACGAAAAAG CGAAGGAAGA ACCAGGGAAC CATACGACGT TAATTCTTGC AATGTTAGCT | 1860 |
| ATTGGCGTGT TCTCTTTAGG GCGGTTTATC AAAATTATTC AATTAAGAAA AAATAATTAA | 1920 |

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 415 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Neisseria meningitidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

| | |
|---|-----|
| TACCGGTACG CTAAATATTG GTGATGTATT GGATATTATG ATTTGGGAAG CGCCGCCAGC | 60 |
| GGTATTGTTT GGTGGTGGCC TTTCTTCGAT GGGCTCGGGT AGTGCGCAAC AAACCAAGTT | 120 |
| GCCGGAGCAA CTGGTGACGG CACGTGGTAC GGTTTCTGTG CCGTTTGTG GCGATATTC | 180 |
| GGTGGTCGGT AAAACGCCTG GTCAGGTTCA GGAAATTATT AAAGGCCGCC TGAAAAAAT | 240 |
| GGCCAATCAG CCGCAAGTGA TGGTGCCTT GGTGCAGAAT AATGCGGCAA ATGTATCGGT | 300 |
| GATTCGCGCA GGCAATAGTG TCGTATGCC GTTGACGGCA GCCGGTGAGC GTGTGTTGGA | 360 |
| TGCGGTGGCT GCGGTAGGTG GTTCAACGGC AAATGTGCAG GATACGAATG TGCAG | 415 |

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 438 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

| | |
|---|-----|
| TCGCTTCTCC AGAAGAAATT TTAGAAACAT ATCTAGAAAA TCCCAAATTA GATAAACCGT | 60 |
| TTATATTATG TGAATACGCA CATGCAATGG GAAATTCACC AGGAGATCTT AATGCATATC | 120 |
| AAACATTAAT TGAAAAATAT GATAGTTTTA TTGGCGGTTT TGTTTGGGAA TGGTGTGATC | 180 |
| ATAGCATTCA GGTTGGGATA AAGGAAGGTA AACCAATTTT TAGATATGGT GGAGATTTTG | 240 |
| GTGAGGCCTT ACATGACGGT AATTTTGTG TTGATGGTAT TGTTTCGCCA GATCGAATTC | 300 |
| CACATGAAGG TTATTATGAG TTAAACATG AACATAGACC TTTGAGATTG GTTAACGAAG | 360 |
| AGGATTATCG GTTTACATTG AAGAATCAAT TTGATTTTAC AAATGCGGAG GATAGTTTGA | 420 |
| TTGTTGAGGG AGAAGCGA | 438 |

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(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 768 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus agalactiae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

| | |
|--|-----|
| ATGAACGTTA CACATATGAT GTATCTATCT GGAAGCTCTAG TGGCTGGTGC ATTGTTATTT | 60 |
| TCACCAGCTG TATTAGAAGT ACATGCTGAT CAAGTGACAA CTCCACAAGT GGTAAATCAT | 120 |
| GTAAATAGTA ATAATCAAGC CCAGCAAATG GCTCAAAAGC TTGATCAAGA TAGCATTTCAG | 180 |
| TTGAGAAATA TCAAAGATAA TGTTCAGGGA ACAGATTATG AAAAACCGGT TAATGAGGCT | 240 |
| ATTACTAGCG TGGAAAAATT AAAGACTTCA TTGCGTGCCA ACCCTGAGAC AGTTTATGAT | 300 |
| TTGAATTCTA TTGGTAGTCG TGTAAGAGCC TTAACAGATG TGATTGAAGC AATCACTTTT | 360 |
| TCAACTCAAC ATTTAACAAA TAAGGTTAGT CAAGCAAATA TTGATATGGG ATTTGGGATA | 420 |
| ACTAAGCTAG TTATTCGCAT TTTAGATCCA TTTGCTTCAG TTGATTCAAT TAAAGCTCAA | 480 |
| GTTAACGATG TAAAGGCATT AGAACAAAAA GTTTTAACTT ATCCTGATT AAAACCAACT | 540 |
| GATAGAGCTA CCATCTATAC AAAATCAAAA CTTGATAAGG AAATCTGGAA TACACGCTTT | 600 |
| ACTAGAGATA AAAAAGTACT TAACGTCAAA GAATTTAAAG TTTACAATAC TTTAAATAAA | 660 |
| GCAATCACAC ATGCTGTTGG AGTTCAGTTG AATCCAAATG TTACGGTACA ACAAGTTGAT | 720 |
| CAAGAGATTG TAACATTACA AGCAGCACTT CAAACAGCAT TAAAATAA | 768 |

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 421 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria meningitidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

- 84 -

ATGAAAGTAG GTTTCGTCGG CTGGCGCGGT ATGGTCGGTT CGGTTTTGAT GCAGCGTATG 60
 AAAGAAGAAA ACGACTTCGC CCACATTCCC GAAGCGTTTT TCTTTACCAC TTCCAACGTC 120
 GGCGGCGCAC GCCCTGATTT CGGTCAGGCG GCTAAAACAT TATTGGACGC GAACAACGTT 180
 GCCGAGCTGG CAAAAATGGA CATCATCGTT ACCTGCCAAG GCGGCGACTA CACCAAATCC 240
 GTCTTCCAAG CCCTGCGCGA CAGCGGCTGG AACGGCTACT GGATTGACGC GGCATCCTCG 300
 CTGCGTATGA AAGACGACGC GATTATCGTC CTCGACCCCG TCAACGCAA CGTCATCGAC 360
 AACGGCCTCA AAAACGGCGT GAAAACTAC ATCGGCGGCA ACTGTACCGT TTCCCTGATG 420
 C 421

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 213 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus gordonii*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

TTCATAGACG CTGAGCACGC TTTGGATCCA TCTTACGCGG CTGCTCTAGG TGTAATATTT 60
 GATGAGCTGT TGCTATCTCA ACCAGATTCT GGTGAGCAAG GTTTAGAAAT TGCAGGAAAA 120
 TTGATTGACT CTGGGGCAGT TGATTAGTT GTCATCGACT CTGTTGCAGC TCTTGTACCA 180
 CGTGCGGAAA TCGATGGAGA TATCGGTGAT AGC 213

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 692 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus mutans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

GGGCCGGAAT CTTCTGGTAA GACAACTGTC GCTCTTCATG CTGCTGCTCA GGCGCAAAAA 60

- 85 -

| | |
|---|-----|
| GATGGCGGTA TTGCCGCTTT CATTGATGCA GAACATGCCC TTGATCCAGC CTATGCTGCT | 120 |
| GCTCTTGGCG TTAATATTGA TGAGCTTTTG CTTTCACAAC CAGATTCAGG AGAACAGGGT | 180 |
| CTTGAAATTG CAGGGAAATT GATTGATTCT GGCCTGTGTTG ATTTAGTTGT TGTGACTCA | 240 |
| GTGGCAGCTT TAGTACCACG TGCGGAGATT GACGGAGATA TTGGTAATAG TCATGTTGGC | 300 |
| TTACAAGCAC GCATGATGAG TCAAGCGATG CGTAAATTAT CAGCTTCAAT CAATAAAACA | 360 |
| AAAACCATTG CTATTTTTAT TAATCAATTG CGGGAAAAAG TTGGTATTAT GTTTGGTAAT | 420 |
| CCAGAAACAA CCCCTGGCGG GCGTGCCTTG AAGTTTTATT CTTCTGTGCG TCTTGATGTC | 480 |
| CGCGGCAATA CTCAAATTAA AGGAACCGGG GAACAAAAAG ACAGCAATAT TGGTAAAGAG | 540 |
| ACCAAAATTA AAGTTGTTAA AAATAAAGTT GCTCCACCAT TTAAGGAAGC TTTTGTAGAA | 600 |
| ATTATATATG GTGAAGGCAT TTCTCGTACA GGTGAATTAG TTAAGATTGC CAGTGATTG | 660 |
| GGAATTATCC AAAAAGCTGG AGCTTGGTAC TC | 692 |

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1204 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pneumoniae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

| | |
|---|-----|
| ATGGCGAAAA AACCAAAAAA ATTAGAAGAA ATTTCAAAAA AATTGGGGC AGAACGTGAA | 60 |
| AAGGCCTTGA ATGACGCTCT TAAATTGATT GAGAAAGACT TTGGTAAAGG ATCAATCATG | 120 |
| CGTTTGGGTG AACGTGCGGA GCAAAAGGTG CAAGTGATGA GCTCAGGTTT TTTAGCTCTT | 180 |
| GACATTGCCC TTGGCTCAGG TGGTTATCCT AAGGGACGTA TCATCGAAAT CTATGGCCCA | 240 |
| GAGTCATCTG GTAAGACAAC GGTGCCCCTT CATGCAGTTG CACAAGCGCA AAAAGAAGGT | 300 |
| GGGATTGCTG CCTTTATCGA TGCGGAACAT GCCCTTGATC CAGCTTATGC TGCGGCCCTT | 360 |
| GGTGTCAATA TTGACGAATT GCTCTTGTCT CAACCAGACT CAGGAGAGCA AGGTCTTGAG | 420 |
| ATTGCGGGAA AATTGATTGA CTCAGGTGCA GTTGATCTTG TCGTAGTCGA CTCAGTTGCT | 480 |
| GCCCTTGTTT CTCGTGCGGA AATTGATGGA GATATCGGAG ATAGCCATGT TGGTTTGCAG | 540 |
| GCTCGTATGA TGAGCCAGGC CATGCGTAAA CTTGGCGCCT CTATCAATAA AACCAAAACA | 600 |

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| | |
|--|------|
| ATTGCCATTT TTATCAACCA ATTGCGTGAA AAAGTTGGAG TGATGTTTGG AAATCCAGAA | 660 |
| ACAACACCCGG GCGGACGTGC TTTGAAATTC TATGCTTCAG TCCGCTTGGA TGTTCGTGGT | 720 |
| AATACACAAA TTAAGGGAAC TGGTGATCAA AAAGAAACCA ATGTCGGTAA AGAAACTAAG | 780 |
| ATTAAGGTTG TAAAAAATAA GGTAGCTCCA CCGTTTAAGG AAGCCGTAGT TGAAATTATG | 840 |
| TACGGAGAAG GAATTTCTAA GACTGGTGAG CTTTGAAGA TTGCAAGCGA TTTGGATATT | 900 |
| ATCAAAAAAG CAGGGGCTTG GTATTCTTAC AAAGATGAAA AAATTGGGCA AGGTTCTGAG | 960 |
| AATGCTAAGA AATACTTGGC AGAGCACCCA GAAATCTTTG ATGAAATTGA TAAGCAAGTC | 1020 |
| CGTTCTAAAT TTGGCTTGAT TGATGGAGAA GAAGTTTCAG AACAAGATAC TGAAAACAAA | 1080 |
| AAAGATGAGC CAAAGAAAGA AGAAGCAGTG AATGAAGAAG TTCCGCTTGA CTTAGGCGAT | 1140 |
| GAAC TTGAAA TCGAAATTGA AGAATAAGCT GTTAAAGCAG TGGAGAAATC CGCTACTTTT | 1200 |
| TCGA | 1204 |

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 981 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pyogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

| | |
|---|-----|
| ATGCGTTCAG GAAGTCTAGC TCTTGATATT GCTTGGATAG CTGGTGGTTA TCCTAAAGGA | 60 |
| CGTATCATCG AAATCTATGG TCCAGAGTCT TCCGGTAAAA CGACTGTGGC TTTACATGCT | 120 |
| GTAGCACAAG CTCAAAAAGA AGGTGGAATC GCAGCCTTTA TCGATGCCGA GCATGCGCTT | 180 |
| GATCCAGCTT ATGCTGCTGC GCTTGGGGTT AATATTGATG AACTTCTCTT GTCTCAACCA | 240 |
| GATTCTGGAG AACAAGGACT TGAAATTGCA GGTAAATTGA TTGATTCTGG TCGGTTGAC | 300 |
| CTGGTTGTTG TCGATTCACT AGCAGCTTTA GTGCCACGTG CTGAAATTGA TGGTGATATT | 360 |
| GGCGATAGCC ATGTCGGATT GCAAGCACGT ATGATGAGTC AGGCCATGCG TAAATTATCA | 420 |
| GCTTCTATTA ATAAAACAAA AACTATCGCA ATCTTTATCA ACCAATTGCG TGAAAAAGTT | 480 |
| GGTGTGATGT TTGGAAATCC TGAAACAACA CCAGGTGGTC GAGCTTTGAA ATTCTATGCT | 540 |
| TCTGTTCCGC TGGATGTGCG TGGAAACAAC CAAATTAAAG GAACTGGTGA CAAAAGATA | 600 |

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| | |
|---|-----|
| GCCAGCATTG GTAAGGAGAC CAAAATCAAG GTTGTTAAAA ACAAGGTCGC TCCGCCATT | 660 |
| AAGGTAGCAG AAGTTGAAAT CATGTATGGG GAAGGTATTT CTCGTACAGG GGAGCTTGTG | 720 |
| AAAATTGCTT CTGATTTGGA CATTATCCAA AAAGCAGGTG CTTGGTTCTC TTATAATGGT | 780 |
| GAGAAGATTG GCCAAGGTTT TGAAAATGCT AAGCGTTATT TGGCCGATCA TCCACAATTG | 840 |
| TTTGATGAAA TCGACCGTAA AGTACGTGTT AAATTTGGTT TGCTTGAAGA AAGCGAAGAA | 900 |
| GAATCTGCTA TGGCAGTAGC ATCAGAAGAA ACCGATGATC TTGCTTTAGA TTTAGATAAT | 960 |
| GGTATTGAAA TTGAAGATTA A | 981 |

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 312 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus salivarius*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

| | |
|---|-----|
| GCGTATGCAC GAGCTCTAGG TGTTAATATC GATGAGCTTC TTTTGTGCA GCCTGATTCT | 60 |
| GGTGAGCAAG GTCTCGAAAT TGCAGGTAAG CTGATTGACT CTGGTGCACT GGATTTAGTT | 120 |
| GTTGTTGACT CAGTTGCGGC CTTCGTACCA CGTGCAGAAA TTGATGGAGA TAGTGGTGAC | 180 |
| AGTCATGTAG GACTTCAAGC GCGTATGATG AGTCAAGCCA TCGGTAAACT TTCTGCATCT | 240 |
| ATTAATAAAA CAAAACGAT TGCTATCTTT ATTAACCACT TCGGTGAAAA AGTTGGTATC | 300 |
| ATGTTTGGTA AC | 312 |

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

| | |
|-----------------------|----|
| CTATGTGGCG CGGTATTATC | 20 |
|-----------------------|----|

(2) INFORMATION FOR SEQ ID NO: 38:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

CGCAGTGTTA TCACTCATGG

20

(2) INFORMATION FOR SEQ ID NO: 39:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

CTGAATGAAG CCATACCAAA

20

(2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

ATCAGCAATA AACCAGCCAG

20

(2) INFORMATION FOR SEQ ID NO: 41:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

TTACCATGAG CGATAACAGC

20

(2) INFORMATION FOR SEQ ID NO: 42:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

CTCATTCACT TCCGTTTCCC

20

(2) INFORMATION FOR SEQ ID NO: 43:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

CAGCTGCTGC AGTGGATGGT

20

(2) INFORMATION FOR SEQ ID NO: 44:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

CGCTCTGCTT TGTATTCCG

20

(2) INFORMATION FOR SEQ ID NO: 45:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

TACGCCAACA TCGTGGAAG

20

(2) INFORMATION FOR SEQ ID NO: 46:

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- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

TTGAATTTGG CTTCTTCGGT

20

(2) INFORMATION FOR SEQ ID NO: 47:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

GGGATACAGA AACGGGACAT

20

(2) INFORMATION FOR SEQ ID NO: 48:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

TAAATCTTTT TCAGGCAGCG

20

(2) INFORMATION FOR SEQ ID NO: 49:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

GATGGTTTGA AGGGTTTATT ATAAG

25

(2) INFORMATION FOR SEQ ID NO: 50:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

AATTTAGTGT GTTTAGAATG GTGAT

25

(2) INFORMATION FOR SEQ ID NO: 51:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 21 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

ACTTCAACAC CTGCTGCTTT C

21

(2) INFORMATION FOR SEQ ID NO: 52:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 21 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

TGACCACTTT TATCAGCAAC C

21

(2) INFORMATION FOR SEQ ID NO: 53:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

GGCAATAGTT GAAATGCTCG

20

(2) INFORMATION FOR SEQ ID NO: 54:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

CAGCTGTTAC AACGGACTGG

20

(2) INFORMATION FOR SEQ ID NO: 55:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

TCTATGATCT CGCAGTCTCC

20

(2) INFORMATION FOR SEQ ID NO: 56:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

ATCGTCACCG TAATCTGCTT

20

(2) INFORMATION FOR SEQ ID NO: 57:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

CATTCTCGAT TGCTTTGCTA

20

(2) INFORMATION FOR SEQ ID NO: 58:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

CCGAAATGCT TCTCAAGATA

20

(2) INFORMATION FOR SEQ ID NO: 59:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

CTGGATTATG GCTACGGAGT

20

(2) INFORMATION FOR SEQ ID NO: 60:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

AGCAGTGTGA TGGTATCCAG

20

(2) INFORMATION FOR SEQ ID NO: 61:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

GACTCTTGAT GAAGTGCTGG

20

(2) INFORMATION FOR SEQ ID NO: 62:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

CTGGTCTATT CCTCGCACTC

20

(2) INFORMATION FOR SEQ ID NO: 63:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

TATGAGAAGG CAGGATTCGT

20

(2) INFORMATION FOR SEQ ID NO: 64:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

GCTTTCTCTC GAAGGCTTGT

20

(2) INFORMATION FOR SEQ ID NO: 65:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

GAGTTGCTGT TCAATGATCC

20

(2) INFORMATION FOR SEQ ID NO: 66:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

GTGTTTGAAC CATGTACACG

20

(2) INFORMATION FOR SEQ ID NO: 67:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

TG TAGAGGTC TAGCCCGTGT

20

(2) INFORMATION FOR SEQ ID NO: 68:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

ACGGGGATAA CGACTGTATG

20

(2) INFORMATION FOR SEQ ID NO: 69:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

ATAAAGATGA TAGGCCGGTG

20

(2) INFORMATION FOR SEQ ID NO: 70:

- 96 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

TGCTGTCATA TTGTCTTGCC

20

(2) INFORMATION FOR SEQ ID NO: 71:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

ATTATCTTCG GCGGTTGCTC

20

(2) INFORMATION FOR SEQ ID NO: 72:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

GACTATCGGC TTCCATTCC

20

(2) INFORMATION FOR SEQ ID NO: 73:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

CGATAGAAGC AGCAGGACAA

20

(2) INFORMATION FOR SEQ ID NO: 74:

- 97 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

CTGATGGATG CGGAAGATAC

20

(2) INFORMATION FOR SEQ ID NO: 75:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 21 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

GCCTTATGTA TGAACAAATG G

21

(2) INFORMATION FOR SEQ ID NO: 76:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

GTGACTTTWG TGATCCCTTT TGA

23

(2) INFORMATION FOR SEQ ID NO: 77:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

TCCAATCATT GCACAAAATC

20

(2) INFORMATION FOR SEQ ID NO: 78:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

AATTCCTCT ATTTGGTGGT

20

(2) INFORMATION FOR SEQ ID NO: 79:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

TCCAAGCCA GTAAAGCTAA

20

(2) INFORMATION FOR SEQ ID NO: 80:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

TGGTTTTTCA ACTTCTTCCA

20

(2) INFORMATION FOR SEQ ID NO: 81:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

TCATAGAATG GATGGCTCAA

20

(2) INFORMATION FOR SEQ ID NO: 82:

- 99 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

AGCTACTATT GCACCATCCC

20

(2) INFORMATION FOR SEQ ID NO: 83:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

CAATAAGGGC ATACCAAAAA TC

22

(2) INFORMATION FOR SEQ ID NO: 84:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

CCTTAACATT TGTGGCATT TC

22

(2) INFORMATION FOR SEQ ID NO: 85:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

TTGGGAAGAT GAAGTTTTTA GA

22

(2) INFORMATION FOR SEQ ID NO: 86:

- 100 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

CCTTTACTCC AATAATTGG CT

22

(2) INFORMATION FOR SEQ ID NO: 87:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

TTTCATCTAT TCAGGATGGG

20

(2) INFORMATION FOR SEQ ID NO: 88:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

GGAGCAACAT TCTTTGTGAC

20

(2) INFORMATION FOR SEQ ID NO: 89:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

TGTGCCTGAA GAAGGTATTG

20

(2) INFORMATION FOR SEQ ID NO: 90:

- 101 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

CGTGTTACTT CACCACCACT

20

- (2) INFORMATION FOR SEQ ID NO: 91:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

TATCTTATCG TTGAGAAGGG ATT

23

- (2) INFORMATION FOR SEQ ID NO: 92:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

CTACACTTGG CTTAGGATGA AA

22

- (2) INFORMATION FOR SEQ ID NO: 93:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

CTATCTGATT GTTGAAGAAG GATT

24

- (2) INFORMATION FOR SEQ ID NO: 94:

- 102 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

GTTTACTCTT GGTTTAGGAT GAAA

24

(2) INFORMATION FOR SEQ ID NO: 95:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

CTTGTTGATC ACGATAATTT CC

22

(2) INFORMATION FOR SEQ ID NO: 96:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

ATCTTTTAGC AAACCCGTAT TC

22

(2) INFORMATION FOR SEQ ID NO: 97:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 27 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

AACAGGTGAA TTATTAGCAC TTGTAAG

27

(2) INFORMATION FOR SEQ ID NO: 98:

- 103 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 27 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

ATTGCTGTTA ATATTTTTTG AGTTGAA

27

(2) INFORMATION FOR SEQ ID NO: 99:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

GTGATCGAAA TCCAGATCC

19

(2) INFORMATION FOR SEQ ID NO: 100:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

ATCCTCGGTT TTCTGGAAG

19

(2) INFORMATION FOR SEQ ID NO: 101:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

CTGGTCATAC ATGTGATGG

19

(2) INFORMATION FOR SEQ ID NO: 102:

- 104 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

GATGTTACCC GAGAGCTTG

19

(2) INFORMATION FOR SEQ ID NO: 103:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

TTAAGCGTGC ATAATAAGCC

20

(2) INFORMATION FOR SEQ ID NO: 104:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

TTGCGATTAC TTCGCCAACT

20

(2) INFORMATION FOR SEQ ID NO: 105:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

TTTACTAAGC TTGCCCCTTC

20

(2) INFORMATION FOR SEQ ID NO: 106:

- 105 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

AAAAGGCAGC AATTATGAGC

20

(2) INFORMATION FOR SEQ ID NO: 107:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:9
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:12
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:15
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:18
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:21
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

AAATGATNA CNGGNGCNGC NCARATGGA

29

(2) INFORMATION FOR SEQ ID NO: 108:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid

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- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:3
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:9
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

CCNACNGTNC KNCCRCCYTC RCG

23

(2) INFORMATION FOR SEQ ID NO: 109:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 29 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:6
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:12
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION:15
- (D) OTHER INFORMATION:/note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature

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(B) LOCATION:18

(D) OTHER INFORMATION:/note= "n = inosine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

CARYTNATHG TNGCNGTNAA YAARATGGA

29

(2) INFORMATION FOR SEQ ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 831 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

| | |
|---|-----|
| ATGAAAAACA CAATACATAT CAACTTCGCT ATTTTTTTTAA TAATTGCAA TATTATCTAC | 60 |
| AGCAGCGCCA GTGCATCAAC AGATATCTCT ACTGTTGCAT CTCCATTATT TGAAGGAACT | 120 |
| GAAGGTTGTT TTTTACTTTA CGATGCATCC ACAAACGCTG AAATTGCTCA ATTCAATAAA | 180 |
| GCAAAGTGTG CAACGCAAAT GGCACCAGAT TCAACTTTCA AGATCGCATT ATCACTTATG | 240 |
| GCATTTGATG CGGAAATAAT AGATCAGAAA ACCATATTCA AATGGGATAA AACCCCCAAA | 300 |
| GGAATGGAGA TCTGGAACAG CAATCATACA CCAAAGACGT GGATGCAATT TTCTGTTGTT | 360 |
| TGGGTTTCGC AAGAAATAAC CAAAAAATT AGATTAAATA AAATCAAGAA TTATCTCAA | 420 |
| GATTTTGATT ATGGAAATCA AGACTTCTCT GGAGATAAAG AAAGAAACAA CGGATTAACA | 480 |
| GAAGCATGGC TCGAAAGTAG CTTAAAAATT TCACCAGAAG AACAAATTCA ATTCCTGCGT | 540 |
| AAAATTATTA ATCACAATCT CCCAGTTAAA AACTCAGCCA TAGAAAACAC CATAGAGAAC | 600 |
| ATGTATCTAC AAGATCTGGA TAATAGTACA AACTGTATG GGAAAAC TGG TGCAGGATTC | 660 |
| ACAGCAAATA GAACCTTACA AAACGGATGG TTTGAAGGGT TTATTATAAG CAAATCAGGA | 720 |
| CATAAATATG TTTTGTGTC CGCACTTACA GGAAACTTGG GGTGGAATTT AACATCAAGC | 780 |
| ATAAAAGCCA AGAAAAATGC GATCACCATT CTAAACACAC TAAATTTATA A | 831 |

(2) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 846 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

| | |
|---|-----|
| TTGAAAAAGT TAATATTTTT AATTGTAATT GCTTTAGTTT TAAGTGCATG TAATTCAAAC | 60 |
| AGTTCACATG CCAAAGAGTT AAATGATTTA GAAAAAAAT ATAATGCTCA TATTGGTGT | 120 |
| TATGCTTTAG ATACTAAAAG TGGTAAGGAA GTAAATTTA ATTCAGATAA GAGATTTGCC | 180 |
| TATGCTTCAA CTTCAAAAGC GATAAATAGT GCTATTTTGT TAGAACAAGT ACCTTATAAT | 240 |
| AAGTTAAATA AAAAAGTACA TATTAACAAA GATGATATAG TTGCTTATTC TCCTATTTTA | 300 |
| GAAAAATATG TAGGAAAAGA TATCACTTTA AAAGCACTTA TTGAGGCTTC AATGACATAT | 360 |
| AGTGATAATA CAGCAAACAA TAAAATTATA AAAGAAATCG GTGGAATCAA AAAAGTTAAA | 420 |
| CAACGTCTAA AAGAACTAGG AGATAAAGTA ACAAATCCAG TTAGATATGA GATAGAATTA | 480 |
| AATTACTATT CACCAAAGAG CAAAAAAGAT ACTTCAACAC CTGCTGCTTT CGGTAAGACT | 540 |
| TTAAATAAAC TTATCGCAAA TGGAAAATTA AGCAAAGAAA ACAAAAAATT CTTACTTGAT | 600 |
| TTAATGTAA ATAATAAAAG CGGAGATACT TTAATTAAAG ACGGTGTTCC AAAAGACTAT | 660 |
| AAGGTTGCTG ATAAAAGTGG TCAAGCAATA ACATATGCTT CTAGAAATGA TGTGCTTTT | 720 |
| GTTTATCCTA AGGGCCAATC TGAACCTATT GTTTTAGTCA TTTTACGAA TAAAGACAAT | 780 |
| AAAAGTGATA AGCCAAATGA TAAGTTGATA AGTGAAACCG CCAAGAGTGT AATGAAGGAA | 840 |
| TTTTAA | 846 |

(2) INFORMATION FOR SEQ ID NO: 112:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 555 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

| | |
|---|-----|
| ATGTCCGCGA GCACCCCCC CATAACTCTT CGCCTCATGA CCGAGCGCGA CCTGCCGATG | 60 |
| CTCCATGACT GGCTCAACCG GCCGCACATC GTTGAGTGGT GGGGTGGCGA CGAAGAGCGA | 120 |
| CCGACTCTTG ATGAAGTGCT GGAACACTAC CTGCCAGAG CGATGGCGGA AGAGTCCGTA | 180 |
| ACACCGTACA TCGCAATGCT GGGCGAGGAA CCGATCGGCT ATGCTCAGTC GTACGTCGCG | 240 |
| CTCGGAAGCG GTGATGGCTG GTGGGAAGAT GAAACTGATC CAGGAGTGCG AGGAATAGAC | 300 |
| CAGTCTCTGG CTGACCCGAC ACAGTTGAAC AAAGGCCTAG GAACAAGGCT TGTCCGCGCT | 360 |

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| | |
|--|-----|
| CTCGTTGAAC TACTGTTCTC GGACCCACCC GTGACGAAGA TTCAGACCGA CCCGACTCCG | 420 |
| AACAACCATC GAGCCATACG CTGCTATGAG AAGGCAGGAT TCGTGCGGGA GAAGATCATC | 480 |
| ACCACGCCTG ACGGGCCGGC GGTTTACATG GTTCAAACAC GACAAGCCTT CGAGAGAAAAG | 540 |
| CGCGGTGTTG CCTAA | 555 |

(2) INFORMATION FOR SEQ ID NO: 113:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

| | |
|---|-----|
| ATGAACCAGA AAAACCCTAA AGACACGCAA AATTTTATTA CTTCTAAAA GCATGTAAAA | 60 |
| GAAATATTGA ATCACACGAA TATCAGTAAA CAAGACAACG TAATAGAAAT CGGATCAGGA | 120 |
| AAAGGACATT TTACCAAAGA GCTAGTCAAA ATGAGTCGAT CAGTTACTGC TATAGAAATT | 180 |
| GATGGAGGCT TATGTCAAGT GACTAAAGAA GCGGTAAACC CCTCTGAGAA TATAAAAGTG | 240 |
| ATTCAAACGG ATATTCTAAA ATTTTCCTTC CCAAACATA TAACTATAA GATATATGGT | 300 |
| AATATTCCTT ATAACATCAG TACGGATATT GTCAAAAGAA TTACCTTTGA AAGTCAGGCT | 360 |
| AAATATAGCT ATCTTATCGT TGAGAAGGGA TTTGCGAAAA GATTGCAAAA TCTGCAACGA | 420 |
| GCTTTGGGTT TACTATTAAT GGTGGAGATG GATATAAAAA TGCTCAAAAA AGTACCACCA | 480 |
| CTATATTTTC ATCCTAAGCC AAGGTAGTAC TCTGTATTGA TTGTTCTTGA ACGACATCAA | 540 |
| CCATTGATTT CAAAGAAGGA CTACAAAAAG TATCGATCTT TTGTTTATAA GTGGGTAAAC | 600 |
| CGTGAATATC GTGTTCTTTT CACTAAAAAC CAATTCCGAC AGGCTTTGAA GCATGCAAAT | 660 |
| GTCACATAA TTAATAAACT ATCGAAGGAA CAATTCTTT CTATTTTCAA TAGTTACAAA | 720 |
| TTGTTTCACT AA | 732 |

(2) INFORMATION FOR SEQ ID NO: 114:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 738 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

| | |
|---|-----|
| ATGAACAAAA ATATAAAATA TTCTCAAAAC TTTTAAACGA GTGAAAAAGT ACTCAACCAA | 60 |
| ATAATAAAAC AATTGAATTT AAAAGAAACC GATACCGTTT ACGAAATTGG AACAGGTAAA | 120 |
| GGGCATTTAA CGACGAAACT GGCTAAAATA AGTAAACAGG TAACGTCTAT TGAATTAGAC | 180 |
| AGTCATCTAT TCAACTTATC GTCAGAAAAA TTAATTCGA ATACTCGTGT CACTTTAATT | 240 |
| CACCAAGATA TTCTACAGTT TCAATTCCCT AACAAACAGA GGTATAAAAT TGTTGGGAAT | 300 |
| ATTCCTTACC ATTTAAGCAC ACAAATTATT AAAAAAGTGG TTTTGAAG CCATGCGTCT | 360 |
| GACATCTATC TGATTGTTGA AGAAGGATTC TACAAGCGTA CCTTGGATAT TCACCGAACA | 420 |
| CTAGGGTTGC TCTTGACAC TCAAGTCTCG ATTCAGCAAT TGCTTAAGCT GCCAGCGGAA | 480 |
| TGCTTTCATC CTAAACCAAG AGTAAACAGT GTCTTAATAA AACTTACCCG CCATACCACA | 540 |
| GATGTTCCAG ATAAATATTG GAAGCTATAT ACGTACTTTG TTTCAAAATG GGTCAATCGA | 600 |
| GAATATCGTC AACTGTTTAC TAAAAATCAG TTTCATCAAG CAATGAAACA CGCCAAAGTA | 660 |
| AACAATTTAA GTACCGTTAC TTATGAGCAA GTATTGTCTA TTTTAAATAG TTATCTATTA | 720 |
| TTTAACGGGA GGAAATAA | 738 |

(2) INFORMATION FOR SEQ ID NO: 115:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 735 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

| | |
|---|-----|
| ATGAACGAGA AAAATATAAA ACACAGTCAA AACTTTATTA CTTCAAAACA TAATATAGAT | 60 |
| AAAATAATGA CAAATATAAG ATTAAATGAA CATGATAATA TCTTTGAAAT CGGCTCAGGA | 120 |
| AAAGGGCATT TTACCCTTGA ATTAGTACAG AGGTGTAATT TCGTAACTGC CATTGAAATA | 180 |
| GACCATAAAT TATGCAAAAC TACAGAAAAT AAATTGTTG ATCACGATAA TTTCCAAGTT | 240 |
| TTAAACAAGG ATATATTGCA GTTTAAATTT CCTAAAACC AATCCTATAA AATATTTGGT | 300 |
| AATATACCTT ATAACATAAG TACGGATATA ATACGCAAAA TTGTTTTTGA TAGTATAGCT | 360 |
| GATGAGATTT ATTTAATCGT GGAATACGGG TTTGCTAAAA GATTATTAA TACAAAACGC | 420 |
| TCATTGGCAT TATTTTAAAT GGCAGAAGTT GATATTTCTA TATTAAGTAT GGTCCAAGA | 480 |

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| | |
|---|-----|
| GAATATTTTC ATCCTAAACC TAGAGTGAAT AGCTCACTTA TCAGATTAAA TAGAAAAAAA | 540 |
| TCAAGAATAT CACACAAAGA TAAACAGAAG TATAATTATT TCGTTATGAA ATGGGTTAAC | 600 |
| AAAGAATACA AGAAAATATT TACAAAAAAT CAATTTAACA ATTCCTTAAA ACATGCAGGA | 660 |
| ATTGACGATT TAAACAATAT TAGCTTTGAA CAATTCTTAT CTCTTTTCAA TAGCTATAAA | 720 |
| TTATTTAATA AGTAA | 735 |

(2) INFORMATION FOR SEQ ID NO: 116:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1029 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

| | |
|---|------|
| ATGAATAAAA TAAAAGTCGC AATTATCTTC GCGGTTGCT CGGAGGAACA TGATGTGTCG | 60 |
| GTAAAATCCG CAATAGAAAT TGCTGCGAAC ATTAATACTG AAAAATTCGA TCCGCACTAC | 120 |
| ATCGGAATTA CAAAAACGG CGTATGGAAG CTATGCAAGA AGCCATGTAC GGAATGGGAA | 180 |
| GCCGATAGTC TCCCCGCCAT ATTCTCCCCG GATAGGAAAA CGCATGGTCT GCTTGTCATG | 240 |
| AAAGAAAGAG AATACGAAAC TCGGCGTATT GACGTGGCTT TCCCGGTTTT GCATGGCAAA | 300 |
| TGCGGGGAGG ATGGTGCGAT ACAGGGTCTG TTTGAATTGT CTGGTATCCC CTATGTAGGC | 360 |
| TGCGATATTC AAAGCTCCGC AGCTTGCATG GACAAATCAC TGGCCTACAT TCTTACAAAA | 420 |
| AATGCGGGCA TCGCCGTCCC CGAATTTCAA ATGATTGAAA AAGGTGACAA ACCGGAGGCG | 480 |
| AGGACGCTTA CCTACCCTGT CTTTGTGAAG CCGGCACGGT CAGGTTTCGT CTTTGGCGTA | 540 |
| ACCAAAGTAA ACGTACGGA AGAACTAAAC GCTGCGATAG AAGCAGCAGG ACAATATGAT | 600 |
| GGAAAAATCT TAATTGAGCA AGCGATTTTC GGCTGTGAGG TCGGCTGCGC GGTCATGGGA | 660 |
| AACGAGGATG ATTTGATTGT CGGCGAAGTG GATCAAATCC GGTTGAGCCA CGGTATCTTC | 720 |
| CGCATCCATC AGGAAAACGA GCCGGAAAAA GGCTCAGAGA ATGCGATGAT TATCGTTCCA | 780 |
| GCAGACATTC CGGTCGAGGA ACGAAATCGG GTGCAAGAAA CGGCAAAGAA AGTATATCGG | 840 |
| GTGCTTGAT GCAGAGGGCT TGCTCGTGTT GATCTTTTTT TGCAGGAGGA TGGCGGCATC | 900 |
| GTTCTAAACG AGGTCAATAC CCTGCCCGGT TTTACATCGT ACAGCCGCTA TCCACGCATG | 960 |
| GCGGCTGCCG CAGGAATCAC GCTTCCCGCA CTAATTGACA GCCTGATTAC ATTGGCGATA | 1020 |

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GAGAGGTGA

1029

(2) INFORMATION FOR SEQ ID NO: 117:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1031 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

| | |
|---|------|
| ATGAAAAAA TTGCCGTTTT ATTTGGAGGG AATTCTCCAG AATACTCAGT GTCACTAACC | 60 |
| TCAGCAGCAA GTGTGATCCA AGCTATTGAC CCGCTGAAAT ATGAAGTAAT GACCATTGGC | 120 |
| ATCGCACCAA CAATGGATTG GTATTGGTAT CAAGGAAACC TCGCGAATGT TCGCAATGAT | 180 |
| ACTTGGCTAG AAGATCACAA AACTGTGCAC CAGCTGACTT TTTCTAGCCA AGGATTTATA | 240 |
| TTAGGAGAAA AACGAATCGT CCCTGATGTC CTCTTCCAG TCTTGCATGG GAAGTATGGC | 300 |
| GAGGATGGCT GTATCCAAGG ACTGCTTGAA CTAATGAACC TGCCTTATGT TGGTTGCCAT | 360 |
| GTCGCTGCCT CCGCATTATG TATGAACAAA TGGCTCTTGC ATCAACTTGC TGATACCATG | 420 |
| GGAATCGCTA GTGCTCCAC TTTGCTTTTA TCCCGCTATG AAAACGATCC TGCCACAATC | 480 |
| GATCGTTTTA TTCAAGACCA TGGATTCCCG ATCTTTATCA AGCCGAATGA AGCCGGTTCT | 540 |
| TCAAAAGGGA TCACAAAAGT AACTGACAAA ACAGCGCTCC AATCTGCATT AACGACTGCT | 600 |
| TTTGCTTACG GTTCTACTGT GTTGATCCAA AAGGCGATAG CGGGTATTGA AATTGGCTGC | 660 |
| GGCATCTTAG GAAATGAGCA ATTGACGATT GGTGCTTGTG ATGCGATTTC TCTGTGCGAC | 720 |
| GGTTTTTTTG ATTTTGAAGA GAAATACCAA TTAATCAGCG CCACGATCAC TGTCCCAGCA | 780 |
| CCATTGCCTC TCGCGCTTGA ATCACAGATC AAGGAGCAGG CACAGCTGCT TTATCGAAAC | 840 |
| TTGGGATTGA CGGGTCTGGC TCGAATCGAT TTTTTCGTCA CCAATCAAGG AGCGATTTAT | 900 |
| TTAAACGAAA TCAACACCAT GCCGGGATTT ACTGGGCACT CCCGCTACCC AGCTATGATG | 960 |
| GCGGAAGTCG GGTTATCCTA CGAAATATTA GTAGAGCAAT TGATTGCACT GGCAGAGGAG | 1020 |
| GACAAACGAT G | 1031 |

(2) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 809 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Abiotrophia adiacens*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

| | |
|---|-----|
| TGGTGCTATC TTAGTAGTAT CTGCAGCTGA TGGTCCAATG CCTCAAACAC GTGAACACAT | 60 |
| CTTATTATCA CGTCAAGTAG GTGTTCTTA CATCGTTGTA TTCTTAAACA AAGTTGACAT | 120 |
| GGTTGACGAT GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTATCAGA | 180 |
| ATACGATTTT CCAGGCGATG ACACTCCAGT TGTTCAGGT TCTGCTTTAC GCGCTTTAGA | 240 |
| AGGCGACGCT TCATACRAAG AAAAAATCTT AGAATTAATG GCTGCTGTTG ACGAATACAT | 300 |
| TCCAACCTCA GAACGYGACG TTGACAAACC ATTCATGATG CCAGTTGAAG ACGTGTCTC | 360 |
| AATCACAGGT CGTGGTACTG TTGCTACAGG TCGTGTGAA CGTGGACAAG TTCGTGTTGG | 420 |
| TGACGAAGTT GAAATCGTTG GTATTTTCTA AGAACTTCA AAAACAACTG TAACTGGTGT | 480 |
| TGAAATGTTT CGTAAATTGT TAGACTACGC TGAAGCAGGG GATAACATTG GTACATTATT | 540 |
| ACGTGGTGTT ACACGTGACA ACATCGAACG TGGACAAAGT CTTGCTAAAC CAGGAACAAT | 600 |
| CACTCCACAT ACTAAATTCA AAGCTGAAGT TTACGTATTA ACTAAGAAG AAGGTGGACG | 660 |
| TCATACTCCA TTCTTCTCTA ACTACCGTCC TCAATTCTAC TTCCGTACAA CAGACATCAC | 720 |
| TGGTGTGTTG GTGTTACCAG AAGGCGTTGA AATGGTAATG CCTGGTGATA ACGTAACTAT | 780 |
| GGAAGTTGAA TTAATTCACC CAGTAGCGA | 809 |

(2) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 817 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Abiotrophia defectiva*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

| | |
|--|-----|
| CGGCGCGATC CTCGTTGTAT CTGCTGCTGA CGGCCCAATG CCACAACTC GTGAACACAT | 60 |
| CCTCTTGTCT CGTCAAGTTG GTGTTCTTA CATCGTAGTA TTCTTGAACA AAGTTGACAT | 120 |

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GGTTGACGAC GAAGAATTGC TCGAATTAGT TGAAATGGAA GTTCGTGACC TCTTGCTCTGA 180
 ATACGACTTC CCAGGCGACG ACACTCCAGT TATCGCTGGT TCAGCTTTGA AAGCTTTAGA 240
 AGGCGACGCT AACTACGAAG CTAAAGTTTT AGAATTGATG GAACAAGTTG ATGCTTACAT 300
 TCCAGAACCA GAACGTGACA CTGACAAGCC ATTCATGATG CCAGTCGAAG ACGTATTCTC 360
 TATCACTGGT CGTGGTACTG TTGCAACTGG TCGTGTTGAA CGTGGTCAAG TTCGCGTTGG 420
 TGACGAAGTT GAAATCGTTG GTATCGAAGA AGAAACTTCT AAGACTACCG TTACCGGTGT 480
 TGAAATGTTT CGTAAGTTAT TGGATTACGC TGAAGCTGGG GACAACGTTG GTACCTTGTT 540
 ACGTGGTGTA ACTCGTGACC AAATCCAACG TGGTCAAGTA TTATCTAAAC CAGGTTCAAT 600
 CACTCCGYAC ACTAAGTTCG AAGCTGAAGT GTACGTATTG TCTAAAGAAG AAGGTGGTCG 660
 TCACACTCCA TTCTTCTCTA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC 720
 TGGTGTGTTT ACTTTACCAG AAGGTACTGA AATGTTATG CCAGGCGACA ACGTACAAAT 780
 GGTGTTTGAA TTGATCCACC CAATCGCGAT CGAAGAA 817

(2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 754 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida albicans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

CTCTGTCAAA TGGGACAAA ACAGATTTGA AGAAATCATC AAGGAAACCT CCAACTTCGT 60
 CAAGAAGGTT GGTTACAACC CAAAGACTGT TCCATTCGTT CCAATCTCTG GTTGGAATGG 120
 TGACAACWTG ATTGAASCAT CCACCAACTG TCCATGGTAC AAGGGTTGGG AAAAGGAAAC 180
 CAAATCCGGT AAAGTTACTG GTAAGACCTT GTTAGAAGCT ATTGACGCTA TTGAACCACC 240
 AACCAGACCA ACCGACAAAC CATTGAGATT GCCATTTRCAA GATGTTTACA AGATCGGTGG 300
 TATTGGTACT GTGCCAGTCG GTAGAGTTGA AACTGGTATC ATCAAAGCCG GTATGGTWGT 360
 TACTTTCGCC CCAGCTGGTG TTACCACTGA AGTCAARTCC GTTGAAATGC ATCACGAACA 420
 ATTGGCTGAA GGTGTTCCAG GTGACAATGT TRGTTTCAAC GTTAAGAACR TTTCCGTTAA 480
 AGAAATTAGA AGAGGTAACG TTTGTGGTGA CTCCAAGAAC GATCCACCAA AGGGTTGTGA 540

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| | |
|---|-----|
| CTCTTTCAAT GCCCAAGTCA TTGTTTTGAA CCATCCAGGT CAAATCTCTG CTGGTTACTC | 600 |
| TCCAGTCTTG GATTGTCACR CTGCCCACAT TGCTTGTAAG TCGACRCTT TGGTTGAAAA | 660 |
| GATTGACAGA AGAACTGGTA AGRAATTGGA AGAAAATCCA AAATTCGTCA AATCCGGTGA | 720 |
| TGCTGCTATC GTCAAGATGG TCCCAACCAA ACCA | 754 |

(2) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 753 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida glabrata*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

| | |
|---|-----|
| TCTGTCAAGT GGGATGAATC CAGATTCGCT GAAATCGTTA AGGAAACCTC CAACTTCATC | 60 |
| AAGAAGGTCG GTTACAACCC AAAGACTGTT CCATTCGTCC CAATCTCTGG TTGGAACGGT | 120 |
| GACAACATGA TTGAAGCCAC CACCAACGCT TCCTGGTACA AGGGTTGGGA AAAGGAAACC | 180 |
| AAGGCTGGTG TCGTCAAGGG TAAGACCTTG TTGGAAGCCA TTGACGCTAT CGAACCACCA | 240 |
| ACCAGACCAA CTGACAAGCC ATTGAGATTG CCATTGCAAG ATGTCTACAA GATCGGTGGT | 300 |
| ATCGGTACGG TGCCAGTCGG TAGAGTCGAA ACCGGTGTCA TCAAGCCAGG TATGGTTGTT | 360 |
| ACCTTCGCCC CAGCTGGTGT TACCACTGAA GTCAAGTCCG TTGAAATGCA CCACGAACAA | 420 |
| TTGACTGAAG GTTTGCCAGG TGACAACGTT GGTTCACAG TTAAGAACGT TTCCGTTAAG | 480 |
| GAAATCAGAA GAGGTAATGT CTGTGGTGAC TCCAAGAAGC ACCCACCAA GGCTGCTGCT | 540 |
| TCTTTCAACG CTACCGTCAT TGTCTTGAAC CACCCAGGTC AAATCTCTGC TGGTTACTCT | 600 |
| CCAGTTTGG ACTGTCACAC CGCCACATT GCTTGTAAGT TCGAAGAATT GTTGGAAGAG | 660 |
| AACGACAGAA GATCCGGTAA GAAGTTGGAA GACTCTCCAA AGTTCTTGAA GTCCGGTGAC | 720 |
| GCTGCTTTGG TTAAGTTCGT TCCATCCAAG CCA | 753 |

(2) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 752 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Candida krusei*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

| | |
|---|-----|
| CCGTTAAGTG GGATGAAAAC AGATTTGAAG AAATTGTCAA GGAAACCCAA AACTTCATCA | 60 |
| AGAAGGTTGG TTACAACCCA AAGACTGTTC CATTCTGTTC AATCTCTGGT TGGAAATGGT | 120 |
| ACAACATGAT TGAAGCATCC ACCAACTGTC CATGGTACAA GGGTTGGACT AAGGAAACCA | 180 |
| AGGCAGGTGT TGTTAAGGGT AAGACCTTAT TAGAAGCAAT CGATGCTATT GAACCACCTG | 240 |
| TCAGACCAAC CGAAAAGCCA TTAAGATTAC CATTACAAGA TGTTTACAAG ATTGGTGGTA | 300 |
| TTGGTACTGT GCCAGTCGGT AGAGTCGAAA CCGGTGTCAT TAAGCCAGGT ATGGTTGTCA | 360 |
| CTTTTGCTCC AGCAGGTGTC ACCACCGAAG TCAAATCCGT TGAAATGCAC CATGAACAAT | 420 |
| TAGAACAAGG TGTTCCAGGT GATAACGTTG GTTTCAACGT TAAGAACGTY TCTGTCAAGG | 480 |
| ATATCAAGAG AGGTAACGTT TGTGGTGAAT CCAAGAACGA CCCACCAATG GGTGCAGCTT | 540 |
| CTTTCAATGC TCAAGTCATT GTCTTGAACC ACCCTGGTCA AATTTCCGCT GGTACTCTC | 600 |
| CAGTCTTGA TTGTCACACT GCCCACATTG CATGTAAGTT CGACGAATTA ATCGAAAAGA | 660 |
| TTGACAGAAG AACTGGTAAG TCTGTTGAAG ACCATCCAAA GTCYGTCAAG TCTGGTGATG | 720 |
| CAGCTATCGT CAAGATGGTC CCAACCAAGC CA | 752 |

(2) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 754 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Candida parapsilosis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

| | |
|---|-----|
| CTCAGTCAAA TGGGACAAGA RCAGATACGA AGAAATTGTC AAGGAAACTT CCAACTTCGT | 60 |
| CAAGAAGGTT GGTTACAACC CTAAAGCTGT CCCATTCTG CCAATCTCTG GTTGAACGG | 120 |
| TGACAATATG ATTGAACCAT CAACCAACTG TCCATGGTAC AAGGGTTGGG AAAAGGAAAC | 180 |
| TAAAGCTGGT AAGGTTACCG GTAAGACCTT GTTGAAGCT ATCGATGCTA TCGARCCACC | 240 |

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| | |
|---|-----|
| AACCAGACCA ACTGACAAGC CATTGAGATT GCCATTGCAA GATGTCTACA AGATTGGTGG | 300 |
| TATTGGAACT GTGCCAGTTG GTAGAGTTGA AACCGGTATC ATCAAGGCTG GTATGGTTGT | 360 |
| TACTTTTGCC CCAGCTGGTG TTACCACTGA AGTCAAGTCC GTTGAAATGC ACCACGAACA | 420 |
| ATTGACTGAA GGTGTCCCAG GTGACAATGT TGGTTTCAAC GTCAAGAACG TTTCAATTAA | 480 |
| GGAAATCAGA AGAGGTAACG TYTGTGGTGA CTCCAAGAAC GATCCACCAA AGGGATGTGA | 540 |
| YTCCTTCAAT GCTCAAGTTA TTGTCTTGAA CCACCCAGGT CAAATCTCTG CTGGTTACTC | 600 |
| ACCAGTCTTG GATTGTCACA CTGCCCACAT TGCTTGTAAT TCGACACTT TGATTGAAAA | 660 |
| GATTGACAGA AGAACCGGTA AGAAATTGGA AGWTGAACCA AAATTCATCA AGTCCGGTGA | 720 |
| TGCTGCTATC GTCAAGATGG TCCCAACCAA GCCA | 754 |

(2) INFORMATION FOR SEQ ID NO: 124:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 753 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Candida tropicalis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

| | |
|---|-----|
| TCTGTTAAAT GGGACAARAA CAGATTTGAA GAAATTATCA AGGAAACYTC TAACTTCGTC | 60 |
| AAGAAGGTTG GTTACAACCC TAAGGCTGTT CCATTCGTTT CAATCTCWGG TTGGAATGGT | 120 |
| GACAACATGA TTGAAGCTTC TACCAACTGT CCATGGTACA AGGGTTGGGA AAAAGAAACC | 180 |
| AAGGCTGGTA AGGTTACCGG TAAGACTTTG TTGGAAGCCA TTGATGCTAT TGAACCACCT | 240 |
| TCAAGACCAA CTGACAAGCC ATTGAGATTG CCATTGCAAG ATGTTTACAA GATTGGTGGT | 300 |
| ATTGGTACTG TGCCAGTCGG TAGAGTTGAA ACTGGTGTCA TCAAAGCCGG TATGGTTGTT | 360 |
| ACTTTYGCCC CAGCTGGTGT TACCACTGAA GTCAAATCCG TYGAAATGCA CCACGAACAA | 420 |
| TTGGCTGAAG GTGTCCCAGG TGACAATGTT GGTTCACACG TTAAGAACGT TTCTGTTAAA | 480 |
| GAAATTAGAA GAGGTAACGT TTGTGGTGAC TCCAAGAACG ATCCACCAA GGGTTGTGAC | 540 |
| TCTTTCAACG CTCAAGTTAT TGTCTTGAAC CACCCAGGTC AAATYTCTGC TGGTTACTCT | 600 |
| CCAGTCTTGG ATTGTCACAC TGCTCATATT GCTTGTAAT TCGACACCTT GGTGAAAAAG | 660 |
| ATTGACAGAA GAACTGGTAA GAAATTGGAA GAAATCCAA AATTCGTCAA ATCCGGTGAT | 720 |

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GCTGCTATTG TCAAGATGGT TCCAACCAAA CCA

753

(2) INFORMATION FOR SEQ ID NO: 125:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium accolens*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

| | |
|---|-----|
| CGGCGCTATC CTGTTTGTG CTGCAACCGA TGGCCCGATG CCGCAGACCC GCGAGCACGT | 60 |
| TCTGCTTGCT CGCCAGGTTG GCGTTCCTTA CATCCTCGTT GCACTGAACA AGTGCGACAT | 120 |
| GGTTGATGAT GAGGAAATCA TCGAGCTCGT GGAGATGGAG ATCTCCGAGC TGCTCGCAGA | 180 |
| GCAGGACTAC GATGAGGAAG CTCCTATCGT TCACATCTCC GCTCTGAAGG CACTCGAGGG | 240 |
| TGACGAGAAG TGGGTACAGT CCATCGTTGA CCTGATGGAT GCCTGCGACA ACTCCATCCC | 300 |
| TGATCCGGAG CGCGCTACCG ATCAGCCGTT CTTGATGCCT ATCGAGGACA TCTTCACCAT | 360 |
| TACCGGCCCG GGTACCGTTG TTACCGGCCG TGTGAGCGT GGTCGTCTGA ACGTCAACGA | 420 |
| GGACGTTGAG ATCATCGGTA TCCAGGAGAA GTCCCAGAAC ACCACCGTTA CCGGTATCGA | 480 |
| GATGTTCCGC AAGATGATGG ACTACACCGA GGCTGGCGAC AACTGTGGTC TGCTTCTGCG | 540 |
| TGGTACCAAG CGTGAGGACG TTGAGCGTGG CCAGGTTGTT ATCAAGCCGG GCGCTTACAC | 600 |
| CCCTCACACC AAGTTCGAGG GTTCCGTCTA CGTCTGAAG AAGGAAGAGG GCGGCCGCCA | 660 |
| CACCCCGYTC ATGAACAACCT ACCGTCTCA GTTCTACTTC CGCACCACCG ACGTTACCGG | 720 |
| TGTTGTGAAC CTGCCTGAGG GCACCGAGAT GGTATGCCT GGCGACAACG TTGAGATGTC | 780 |
| TGTTGAGCTC ATCCAGCCTG TTGCTATGGA CGAG | 814 |

(2) INFORMATION FOR SEQ ID NO: 126:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Corynebacterium diphtheriae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

| | |
|---|-----|
| CGGCGCAATC CTCGTTGTTG CTGCCACCGA CGGCCCAATG CCTCAGACCC GTGAGCACGT | 60 |
| TCTGCTCGCT CGCCAGGTCG GCGTTCCTTA CATCCTCGTT GCTCTGAACA AGTGCGACAT | 120 |
| GGTTGATGAT GAGGAAATCA TCGAGCTCGT CGAGATGGAG ATCCRTGAGC TGCTCGCTGA | 180 |
| GCAGGATTAC GACGAAGAGG CTCCAATCAT CCACATCTCC GCACTGAAGG CTCTTGAGGG | 240 |
| CGACGAGAAG TGGACCCAGT CCATCATCGA CCTCATGCAG GCTTGCKATG ATTCCATCCC | 300 |
| AGACCCAGAG CGTGAGACCG ACAAGCCATT CCTCATGCCT ATCGAGGACA TCTTCACCAT | 360 |
| CACCGGCCGC GGTACCGTTG TTACCGGCCG TGTGAGCGT GGCTCCCTGA AGGTCAACGA | 420 |
| GGACGTCGAG ATCATCGGTA TCCGCGAGAA KGCTACCACC ACCACCGTTA CCGGTATCGA | 480 |
| GATGTTCCGT AAGCTTCTCG ACTACACCGA GGCTGGCGAC AACTGTGGTC TGCTTCTCCG | 540 |
| TGGCGTTAAG CGCGAAGACG TTGAGCGTGG CCAGGTTGTT GTTAAGCCAG GCGCTTACAC | 600 |
| CCCTCACACC GAGTTCGAGG GCTCTGTCTA CGTTCGTGCC AAGGACGAGG GTGGCCGCCA | 660 |
| CACCCCATTC TTCGACAACT ACCGCCCACA GTTCTACTTC CGCACCACCG ACGTTACCGG | 720 |
| TGTTGTGAAG CTTCTGAGG GCACCGAGAT GGTATGCCT GCGACAACG TCGACATGTC | 780 |
| CGTCACCCTG ATCCAGCCTG TCGCTATGGA TGAG | 814 |

(2) INFORMATION FOR SEQ ID NO: 127:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Corynebacterium genitalium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

| | |
|---|-----|
| CGGCGCCATC CTGTTGTTG CTGCAACCGA TGGCCCAGATG CCGCAGACCC GTGAGCACGT | 60 |
| TCTGCTGGCT CGCCAGGTTG GCGTTCGTA CATCCTAGTT GCACTGAACA AGTGCGACAT | 120 |
| GGTTGATGAT GAGGAGCTGC TGGAGCTCGT CGAGATGGAG GTCCGCGAGC TGCTGGCTGA | 180 |
| GCAGGACTTC GACGAGGAAG CACCTGTTGT TCACATCTCC GCACTGAAGG CCCTGGAGGG | 240 |
| CGACGAGAAG TGGGCTAAGC AGATCCTGGA GTCATGGAG GCTTGCGACA ACTCCATCCC | 300 |

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| | |
|---|-----|
| GGATCCGGAG CGCGAGACCG ACAAGCCGTT CCTGATGCCG GTTGRGGACA TCTTCACCAT | 360 |
| TACCGGCCGC GGTACCGTTG TTACCGGCCG TGTGAGCGT GGCCTCCTGA ACCTGAACGA | 420 |
| CGAGGTCGAG ATCCTGGGCA TCCGCGAGAA GTCCACCAAG ACCACCGTTA CCTCCATCGA | 480 |
| GATGTTCAAC AAGCTGCTGG ACACCGCAGA GGCTGGCGAC AACGCCGCAC TGCTGCTGCG | 540 |
| TGGCCTGAAG CGCGAAGATG TTGAGCGTGG TCAGATCGTT GCTAAGCCGG GCGAGTACAC | 600 |
| CCCGCACACC GAGTTCGAGG GCTCCGTCTA CGTTCTGTCC AAGGACGAGG GTGGCCGCCA | 660 |
| CACCCCGTTC TTCGACAACT ACCGTCCGCA GTTCTATTTT CGCACCACCG ACGTTACCGG | 720 |
| TGTTGTGAAG CTGCCGGAGG GCACCGAGAT GGTATGCCG GCGACAACG TTGACATGTC | 780 |
| CGTCACCCTG ATCCAGCCGG TTGCTATGGA CGAG | 814 |

(2) INFORMATION FOR SEQ ID NO: 128:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium jeikeium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

| | |
|---|-----|
| CGGCGCCATC CTGGTTGTTG CCGCAACCGA TGGCCCGATG CCGCAGACCC GCGAGCACGT | 60 |
| TCTGCTGGCY CGCCAGGTTG GCGTTCCGTA CATCCTGGTT GCACTGAACA AGTGTGACAT | 120 |
| GGTTGACGAT GAGGAGCTGC TGGAGCTCGT CGAGATGGAG GTCCGCGAGC TGCTGGCTGA | 180 |
| GCAGGACTTC GACGAGGAAG CTCGGGTTGT TCACATCTCC GCACTGAAGG CCCTGGAGGG | 240 |
| CGACGAGAAG TGGGCTAACC AGATTCTCGA GCTGATGCAG GCTTGCGACG AGTCTATCCC | 300 |
| GGATCCGGAG CGCGAGACCG ACAAGCCGTT CCTGATGCCG GTTGWGGACA TCTTCACCAT | 360 |
| TACCGGTCGC GGTACCGTTG TTACCGGCCG TGTGAGCGT GGCATCCTGA ACCTGAACGA | 420 |
| CGAGGTTGAG ATCCTGGGTA TCCGCGAGAA GTCCAGAAG ACCACCGTTA CCTCCATCGA | 480 |
| GATGTTCAAC AAGCTGCTGG ACACCGCAGA GGCTGGCRAC AACGCTGCAC TGCTGCTGCG | 540 |
| TGGTCTGAAG CGCGAGGACG TTGAGCGTGG CCAGATCATC GCTAAGCCGG GCGAGTACAC | 600 |
| CCCGCACACC GAGTTCGAGG GCTCCGTCTA CGTTCTGTCC AAGGACGAGG GCGGCCGCCA | 660 |
| CACCCCGTTC TTCGACAACT ACCGTCCGCA GTTCTACTTC CGCACCACCG ACGTTACCGG | 720 |

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TGTTGTGAAG CTGCCTGAGG GCACCGAGAT GGTATGCCG GGCGACAACG TYGACATGTC 780
 CGTCACCCTG ATCCAGCCGG TTGCTATGGA CGAG 814

(2) INFORMATION FOR SEQ ID NO: 129:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 748 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Corynebacterium pseudodiphtheriticum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

CGGCGCTATC TTGGTTGTTG CAGCTACCGA CGGCCCAATG CCACAGACTC GCGAGCACGT 60
 TCTGCTGGCT CGCCAGGTTG GCGTTCCTTA CATCCTGGTT GCACTAAACA AGTGCGACAT 120
 GGTGACGAC GAGGAAATCC TCGAGCTCGT CGAGATGGAG ATCCGCGAAT TGCTGGCTGA 180
 CCAGGAATTC GACGAAGAAG CTCCAATCGT TCACATCTCC GCAGTCGGCG CCTTGGAAGG 240
 CGAAGAGAGG TGGGTTAACG CCATCGTTGA ACTGATGGAT GCTTGTGACG AGTCGATCCC 300
 TGATCCAGAC CGTGCTACCG ACAAGCCATT CCTGATGCCT ATCGAGGACA TCTTCACCAT 360
 TACCGGTCGT GGCACCGTTG TTACGGGTCG TGTTGAGCGT GGTTCCTGA AGGTCAACGA 420
 AGAAGTCGAG ATCATCGGCA TCAAGGAAAA GTCCCAGAAG ACCACCATCA CCGGTATCGA 480
 AATGTTCCGC AAGATGCTGG ACTACACCGA GGCCGGCGAC AACGCTGGTC TGCTGCTTCG 540
 CGGTACCAAG CGTGAAGACG TTGAGCGTGG ACAGGTTATC GTTGCTCCAG GTGCTTACAG 600
 CACCCACAAG AAGTTCGAAG GTTCCGTCTA CGTTCTTTCC AAGGACGAGG GCGGCCGCCA 660
 CACCCCGTTC TTCGACAAC TACCGTCCTCA GTTCTACTTC CGCACCACCG ACGTTACCGG 720
 TGTGTTTACC CTGCCTGAGG GCACCGAG 748

(2) INFORMATION FOR SEQ ID NO: 130:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 813 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Corynebacterium striatum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

| | |
|---|-----|
| GGCGCTATCT TGGTTGTTGC TGCAACCGAT GGCCCGRTGC CGCAGACCCG CGAGCACGTT | 60 |
| CTTCTGGCTC GCCAGGTTGG CGTTCCTTAC ATCCTCGTTG CACTGAACAA GTGCGACATG | 120 |
| GTTGACGACG AGGAAATTAT CGAGCTCGTC GAGATGGAGA TCCGCGAACT GCTCGCAGAG | 180 |
| CAGGACTACG ATGAGGAAGC TCCGATCGTT CACATCTCTG CTCTGAAGGC TCTTGAGGGC | 240 |
| GRCGAGAAGT GGGTACAGGC TATCGTTGAC CTGATGCAGG CTTGCGATGA CTCCATCCCG | 300 |
| GATCCGGAGC GCGAGCTGGA CAAGCCGTTT CTGATGCCAA TCGAGGACAT CTTCAACATC | 360 |
| ACCGGCCGCG GTACCGTTGT TACTGGCCGT GTTGAGCGTG GCTCCCTGAA CGTCAACGAG | 420 |
| GACGTTGAGA TCATCGGTAT CCAGGACARG TCCATCTCCA CCACCGTTAC CGGTATCGAG | 480 |
| ATGYTCCGCA AGATGATGGA CTACACCGAG GCTGGCGACA ACTGTGGTCT GCTTCTGCGT | 540 |
| GGTACCAAGC GTGAAGAGGT TGAGCGCGGC CAGGTTGTTA TTAAGCCGGG CGCTTACACC | 600 |
| CCTCACACCC AGTTCGAGGG TTCCGTCTAC GTCCTGAAGA AGGAAGAGGG CGGCCGCCAC | 660 |
| ACCCCGTTCA TGGACAATA CCGTCCGAG TTCTACTTCC GCACCACCGA CGTTACCGGC | 720 |
| GTCATCAAGC TGCCTGAGGG CACCGAGATG GTTATGCCTG GCGACAACGT CGAGATGTCY | 780 |
| GTGAGCTGA TCCAGCCGGT CGCTATGGAC GAG | 813 |

(2) INFORMATION FOR SEQ ID NO: 131:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Enterococcus avium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

| | |
|---|-----|
| CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCTATG CCTCAAATC GTGAACACAT | 60 |
| CTTGTTATCT CGTAACGTTG GTGTTCTTA CATCGTTGTA TTCTTAAACA AAATGGATAT | 120 |
| GGTTGACGAT GAAGAATTAC TTGAATTAGT TGAAATGGAA GTTCGTGACT TATTAAGTGA | 180 |
| ATACGACTTC CCAGGCGACG AACTCCAGT TATCGCAGGT TCAGCGTTGA AAGCTTTAGA | 240 |
| AGGCGACGCT TCATACGAAG AAAAAATCTT AGAATTAATG GCTGCTGTTG ACGAATATAT | 300 |

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| | |
|---|-----|
| CCCAACACCA GTTCGTGATA CTGACAAACC ATTCATGATG CCAGTCGAAG ACGTATTCTC | 360 |
| AATCACTGGT CGTGGTACTG TTGCAACTGG TCGTGTGAA CGTGGACAAG TTCGCGTTGG | 420 |
| TGACGAAGTT GAAATCGTAG GTATCGCTGA CGAAACTGCT AAAACAACTG TTACAGGTGT | 480 |
| TGAAATGTTT CGTAAATTGT TAGACTACGC TGAAGCAGGT GACAACATCG GTGCTTTGTT | 540 |
| ACGTGGTGGT GCACGTGAAG ATATCCAACG TGGACAAGTA TTGGCTAAAC CAGCTTCAAT | 600 |
| CACTCCACAT AAAAAATTCT CTGCAGAAGT TTATGTTCTA ACTAAGAAG AAGGTGGACG | 660 |
| TCATACTCCA TTCTTCACTA ACTACCGTCC TCAGTTCTAC TTCCGTACAA CTGACGTAAC | 720 |
| TGGTGTAGTT GATCTACCAG AAGGTACTGA AATGGTWATG CCTGGGGATA ACGTAACTAT | 780 |
| GGAAGTTGAA TTGATYCACC CAATYCGCGT AGAAGAC | 817 |

(2) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Enterococcus faecalis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

| | |
|---|-----|
| CGGAGCTATC TTAGTAGTTT CTGCTGCTGA TGGTCCTATG CCTCAAACAC GTGAACATAT | 60 |
| CTTATTATCA CGTAACGTTG GTGTACCATA CATCGTTGTA TTCTTAAACA AAATGGATAT | 120 |
| GTTTGATGAC GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTATCAGA | 180 |
| ATACGATTTT CCAGGCGATG ATGTTCCAGT TATCGCAGGT TCTGCTTTGA AAGCTTTAGA | 240 |
| AGGCGACGAG TCTTATGAAG AAAAAATCTT AGAATTAATG GCTGCAGTTG ACGAATATAT | 300 |
| CCCAACTCCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTCGAAG ACGTATTCTC | 360 |
| AATCACTGGA CGTGGTACTG TTGCTACAGG ACGTGTGAA CGTGGTGAAG TTCGCGTTGG | 420 |
| TGACGAAGTT GAAATCGTTG GTATTAAAGA CGAAACATCT AAAACAACYG TTACAGGTGT | 480 |
| TGAAATGTTT CGTAAATTAT TAGACTACGC TGAAGCAGGC GACAACMTCG GTGCTTTATT | 540 |
| ACGTGGTGTA GCACGTGAAG ATATCGAACG TGGACAAGTA TTAGCTAAAC CAGCTACAA | 600 |
| CACTCCACAC AAAAAATTCA AAGCTGAAGT ATACGTATTA TCAAAAGAAG AAGGCGGACG | 660 |
| TCACACTCCA TTCTTCACTA ACTACCGTCC TCAATTCTAC TTCCGTACAA CAGACGTTAC | 720 |

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TGGTGTGTA GAATTGCCAG AAGGTACTGA AATGGTAATG CCTGGTGATA ACGTTGCTAT 780
 GGACGTTGAA TTAATTCACC CAATCGCTAT CGAAGAC 817

(2) INFORMATION FOR SEQ ID NO: 133:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 774 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Enterococcus faecium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

CGGAGCTATC TTGGTAGTTT CTGCTGCTGA CGGCCCAATG CCTCAAACCTC GTGAACACAT 60
 CCTATTGTCT CGTCAAGTTG GTGTTCCCTTA CATCGTTGTA TTCTTGAACA AAGTAGACAT 120
 GGTGATGAC GAAGAATTAC TAGAATTAGT TGAAATGGAA GTTCGTGACC TATTAACAGA 180
 ATACRAATTC CCTGGTGRCG ATGTTCCCTGT AGTTGCTGGA TCAGCTTTGA AAGCTCTAGA 240
 AGGCGACGCT TCATACGAAG AAAAAATTCT TGAATTAATG GCTGCAGTTG ACGAATACAT 300
 CCCAACTCCA GAACGTGACA ACGACAAACC ATTCATGATG CCAGTTGAAG ACGTGTTCTC 360
 AATTACTGGA CGTGGTACTG TTGCTACAGG TCGTGTGAA CGTGGACAAG TTCGCGTTGG 420
 TGACGAAGTT GAAGTTGTTG GTATTGCTGA AGAACTTCA AAAACAACAG TTACTGGTGT 480
 TGAAATGTTT CGTAAATTGT TAGACYACGC TGAAGCTGGA GACRACATTG GTGCTTTACT 540
 ACGTGGTGTT GCACGTGAAG ACATCCAACG TGGACAAGTT TTAGCTAAAC CAGGTACAAT 600
 CACACCTCRT AAAAAATTCT CTGCAGAAGT ATACGTGTTG ACAAAGAAG AAGGTGGACG 660
 TCATACTCCA TTCTTCACTA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC 720
 AGGTGTTGTT GAATTACCAG AAGGAACTGA AATGGTCATG CCCGGTGACA ACGT 774

(2) INFORMATION FOR SEQ ID NO: 134:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 809 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Enterococcus gallinarum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

| | |
|--|-----|
| CGGTGCGATC TTAGTAGTAT CTGCTGCTGA CGGTCCTATG CCTCAAACCTC GTGAACACAT | 60 |
| CTTGTTATCA CGTAACGTTG GCGTACCATA CATCGTTGTT TTCTTGAACA AAATGGATAT | 120 |
| GGTTGAYGAC GAAGAATTGC TAGAATTAGT TGAAATGGAA GTTCGTGACC TATTGTCTGA | 180 |
| ATATGACTTC CCAGGCGACG ATGTTCTGT AATCGCCGGT TCTGCTTTGA AAGCTCTTGA | 240 |
| AGGAGATCCT TCATACGAAG AAAAAATCAT GGAATTGATG GCTGCAGTTG ACGAATACGT | 300 |
| TCCAACCTCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTCGAAG ACGTATTCTC | 360 |
| AATCACTGGA CGTGGTACTG TTGCTACAGG CCGTGTTGAA CGTGGACAAG TTCGCGTTGG | 420 |
| TGATGAAGTA GAAATCGTTG GTATTGCTGA CGAACTGCT AAAACAACTG TAACAGGTGT | 480 |
| TGAAATGTTT CGTAAATTGT TAGACTATGC TGAAGCAGGG GATAACATTG GTGCATTGCT | 540 |
| ACGTGGGGTT GTCGTGAAG ACATCCAACG TGGACAAGTA TTGGCTAAAG CTGGTACAAT | 600 |
| CACACCTCAT ACAAATTCA AAGCTGAAGT TTATGTTTGA ACAAAGAAG AAGGTGGACG | 660 |
| TCACACTCCA TTCTTCACTA ACTACCGTCC TCAGTTCTAC TTCCGTACAA CTGACGTAAC | 720 |
| TGGTGTGTTT GAATTACCAG AAGGAACTGA AATGGTGATG CCTGGCGACA ACGTGACCAT | 780 |
| CGACGTTGAA TTGATRCACC CAATCGCTC | 809 |

(2) INFORMATION FOR SEQ ID NO: 135:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 823 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Gardnerella vaginalis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

| | |
|---|-----|
| TGGCGCAATC CTCGTGGTTG CTGCTACCGA CGGTCCAATG GCTCAGACCC GTGAACACGT | 60 |
| CTTGCTTGCT AAGCAGGTCG GCGTTCCAAA AATTCTTGTT GCTTTGAACA AGTGCGATAT | 120 |
| GGTTGACGAC GAAGAGCTTA TCGATCTCGT TGAAGAAGAG GTCCGTGACC TCCTCGAAGA | 180 |
| AAACGGCTTC GATCGCGATT GCCCAGTCYT CCGTACTTCC GCTTACGGCG CTTTGCATGA | 240 |
| TGACGCTCCA GACCACGACA AGTGGGTAGA GACCGTCAAG GAACTCATGA AGGCTGTTGA | 300 |

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| | |
|--|-----|
| CGAGTACATC CCAACCCCAA CTCACGATCT TGACAAGCCA TTCTTGATGC CAATCGAAGA | 360 |
| TGTGTTCCACC ATCTCCGGTC GTGGTYCCGT TGTCACCGGT CGTGTTGAGC GTGGTAAGCT | 420 |
| CCCAATCAAC ACCCCAGTTG AGATCGTTGG TTTGCGCGAT ACCCAGACCA CCACCGTCAC | 480 |
| CTCTATCGAG ACCTTCCACA AGCAGATGGA TGAGGCAGAG GCTGGCGATA ACACTGGTCT | 540 |
| TCTTCTCCGC GGTATCAACC GTACCGACGT TGAGCGTGGT CAGGTTGTGG CTGCTCCAGG | 600 |
| TTCTGTGACT CCACACACCA AGTTCGAAGG CGAAGTTTAC GTCTTGACCA AGGACGAAGG | 660 |
| TGGCCGTCAC TCGCCATTCT TCTCCAACTA CCGTCCACAG TTCTACTTCC GTACCACCGA | 720 |
| TGTTACTGGC GTTATCACCT TGCCAGACGG CATCGAAATG GTTCAGCCAG GCGATCACGC | 780 |
| AACCTTCACT GTTGAGTTGA TCCAGGCTAT CGCAATGGAA GAG | 823 |

(2) INFORMATION FOR SEQ ID NO: 136:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Listeria innocua*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

| | |
|---|-----|
| CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACATAT | 60 |
| CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT | 120 |
| GGTTGACGAT GAAGAATTAC TAGAATTAGT TGAAATGGAA ATTCGTGATC TATTAACTGA | 180 |
| ATATGAATTC CCTGGCGATG ACATTCCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA | 240 |
| AGGTGAAGCT GACTGGGAAG CTAAAATTGA CGAGTTAATG GAAGCTGTAG ATTCTTACAT | 300 |
| TCCAACCTCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTTGAGG ATGTATTCTC | 360 |
| AATCACTGGT CGTGGAACAG TTGCAACTGG ACGTGTGAA CGTGGACAAG TTAAAGTTGG | 420 |
| TGACGAAGTA GAAGTTATCG GTATTGAAGA AGAAAGCAAA AAAGTAGTAG TAACTGGAGT | 480 |
| AGAAATGTTC CGTAAATTAC TAGACTACGC TGAAGCTGGC GACAACATTG GCGCACTTCT | 540 |
| ACGTGGTGTT GTCGTGAAG ATATCCAACG TGGTCAAGTA TTAGCTAAAC CAGGTTCGAT | 600 |
| TACTCCACAC ACTAACTTCA AAGCTGAAAC TTATGTTTTA ACTAAAGAAG AAGGTGGACG | 660 |
| TCACACTCCA TTCTTCAACA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC | 720 |

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TGGTATTGTT ACACTTCCAG AAGGTACTGA AATGGTAATG CCTGGTGATA ACATTGAGCT 780
 TGCAGTTGAA CTAATTGCAC CAATCGCTAT CGAAGAC 817

(2) INFORMATION FOR SEQ ID NO: 137:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 818 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Listeria ivanovii*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGTCCAATG CCACAAACTC GTGAACATAT 60
 TCTTACTTTC ACGTCAAGTT GGTGTTCCAT ACATCGTTGT ATTCATGAAC AAATGTGACA 120
 TGGTTGACGA TGAAGAATTA CTTGAATTAG TTGAAATGGA AATTCGTGAT CTATTAAGTG 180
 AATATGAATT CCCTGGCGAC GACATTCCTG TAATCAAAGG TTCAGCTCTT AAAGCACTTC 240
 AAGGTGAAGC TGATTGGGAA GCTAAATTTG ACGAGTTAAT GGAAGCTGTA GATTCTTACA 300
 TTCCAAGTCC AGAACGTGAT ACTGACAAAC CATTATGAT GCCAGTTGAG GATGTATTCT 360
 CAATCACTGG TCGTGAACA GTTGCAACTG GACGTGTTGA ACGTGGACAA GTTAAAGTTG 420
 GTGACGAAGT AGAAGTTATC GGTATTGAAG AAGAAAGCAA AAAAGTAGTA GTAAGTGGAG 480
 TAGAAATGTT CCGTAAATTA CTAGACTACG CTGAAGCTGG CGACAACATT GGCGCACTTC 540
 TACGTGGTGT TGCTCGTGAA GATATCCAAC GTGGTCAAGT ATTAGCTAAA CCAGGTTCTGA 600
 TTAAGTCCACA TACTAAGTTC AAAGCTGAAA CTTATGTTTT AACTAAAGAA GAAGGTGGAC 660
 GTCATACTCC ATTCTTCAAC AACTACCGCC CACAATTCTA TTTCCGTACT ACTGACGTAA 720
 CTGGTATTGT TAACTTCCA GAAGGTACTG AAATGGTAAT GCCTGGTGAT AACATTGAGC 780
 TTGCAGTTGA ACTAATTGCA CCAATCGCTA TCGAAGAC 818

(2) INFORMATION FOR SEQ ID NO: 138:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria monocytogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

| | |
|--|-----|
| CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAACTC GTGAACATAT | 60 |
| CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT | 120 |
| GGTTGACGAT GAAGAATTAC TAGAATTAGT TGAAATGGAA ATTCGTGATC TATTAACCTGA | 180 |
| ATATGAATTC CCTGGCGATG ACATTCCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA | 240 |
| AGGTGAAGCT GACTGGGAAG CTAAAATTGA CGAGTTAATG GAAGCTGTAG ATTCTTACAT | 300 |
| TCCAACCTCCW GAACGTGATA CTGACAAACC ATTCATGATG CCAGTTGAGG ATGTATTCTC | 360 |
| AATCACTGGT CGTGGAACAG TTGCAACTGG ACGTGTGAA CGTGGAACAAG TTAAAGTTGG | 420 |
| TGACGAAGTA GAAGTTATCG GTATCGAAGA AGAAAGCAAA AAAGTAGTAG TAACTGGAGT | 480 |
| AGAAATGTTT CGTAAATTAC TAGACTACGC TGAAGCTGGC GACAACATTG GCGCACTTCT | 540 |
| ACGTGGTGTT GTCCTGAAG ATATCCAACR TGGTCAAGTA TTAGCTAAAC CAGGTTTCGAT | 600 |
| TACTCCACAC ACTAACTTCA AAGCTGAAAC TTATGTTTTA ACTAAAGAAG AAGGTGGACG | 660 |
| TCACACTCCA TTCTTCAACA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC | 720 |
| TGGTATTGTT ACACTTCCAG AAGGTACTGA AATGGTAAYG CCTGGTGATA ACATTGAGCT | 780 |
| TGCAGTTGAA CTAATTGCAC CAATCGCTAT CGAAGAC | 817 |

(2) INFORMATION FOR SEQ ID NO: 139:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Listeria seeligeri*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

| | |
|--|-----|
| CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAACTC GTGAACATAT | 60 |
| CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT | 120 |
| GGTTGACGAT GAAGAATTAC TTGAATTAGT TGAAATGGAA ATTCGTGATC TATTAACCTGA | 180 |
| ATATGAATTC CCTGGTGATG ACATTCCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA | 240 |

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AGGTGAAGCT GACTGGGAAG CTAAAATTGA CGAGTTAATG GAAGCTGTAG ATTCTTACAT 300
 TCCAACCTCCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTTGAGG ATGTATTCTC 360
 AATCACTGGT CGTGGAAGT TGTCAACTGG ACGTGTTGAA CGTGGACAAG TTAAAGTTGG 420
 TGACGAAGTA GAAGTTATCG GTATTGAAGA AGAAAGCAAA AAAGTAATAG TAACTGGAGT 480
 AGAAATGTTC CGTAAATTAC TAGACTACGC TGAAGCTGGC GACAACATTG GCGCACTTCT 540
 ACGTGGTGTG GCTCGTGAAG ATATCCAACG TGGTCAAGTA TTAGCTAAAC CAGGTTTCGAT 600
 TACTCCACAT ACTAACTTCA AAGCTGAAAC TTATGTTTTA ACTAAAGAAG AAGGTGGACG 660
 TCACACTCCA TTCTTCAACA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC 720
 TGGTATTGTT ACACCTCCAG AAGGTACTGA AATGGTAATG CCTGGTGATA ACATTGAGCT 780
 TGCAGTTGAA CTAATTGCAC CAATCGCTAT CGAAGAC 817

(2) INFORMATION FOR SEQ ID NO: 140:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Staphylococcus aureus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

CGGTGGTATC TTAGTAGTAT CTGCTGCTGA CGGTCCAATG CCACAACTC GTGAACACAT 60
 TCTTTTATCA CGTAACGTTG GTGTACCAGC ATTAGTAGTA TTCTTAAACA AAGTTGACAT 120
 GGTTGACGAT GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTAAGCGA 180
 ATATGACTTC CCAGGTGACG ATGTACCTGT AATCGCTGGT TCAGCATTAR AAGCTTTAGA 240
 AGGCGATGCT CAATACGAAG AAAAAATCTT AGAATTARTG GAAGCTGTAG ATACTTACAT 300
 TCCAACCTCCA GAACGTGATT CTGACAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC 360
 AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTTGAA CGTGGTCAAA TCAAAGTTGG 420
 TGAAGAAGTT GAAATCATCG GTTTACATGA CACATCTAAA ACAACTGTTA CAGGTGTTGA 480
 AATGTTCCGT AAATTATTAG ACTACGCTGA AGCTGGTGAC AACATTGGTG CATTATTACG 540
 TGGTGTGCT CGTGAAGACG TACAACGTGG TCAAGTATTA GCTGCTCCTG GTTCAATTAC 600
 ACCACATACT GAATTCAAAG CAGAAGTATA CGTATTATCA AAAGACGAAG GTGGACGTCA 660

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CACTCCATTC TTCTCAAAC ATCGTCCACA ATTCTATTTT CGTACTACTG ACGTAACTGG 720
 TGTGTGTTAC TTACCAGAAG GTACTGAAAT GGTAATGCCT GGTGATAACG TTGAAATGAC 780
 AGTAGAATTA ATCGCTCCAA TCGCGATTGA AGAC 814

(2) INFORMATION FOR SEQ ID NO: 141:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Staphylococcus epidermidis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

CGGCGGTATC TTAGTTGTAT CTGCTGCTGA CGGTCCAATG CCACAAACTC GTGAACACAT 60
 CTTATTATCA CGTAACGTTG GTGTACCAGC ATTAGTTGTA TTCTTAAACA AAGTTGACAT 120
 GGTAGACGAC GAAGAATTAT TAGAATTAGT TGAAATGGAA GTTCGTGACT TATTAAGCGA 180
 ATATGACTTC CCAGGTGACG ATGTACCTGT AATCGCTGGT TCTGCATTAA AAGCATTAGA 240
 AGGCGATGCT GAATACGAAC AAAAAATCTT AGACTTAATG CAAGCAGTTG ATGATTACAT 300
 TCCAACTCCA GAACGTGATT CTGACAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC 360
 AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTTGAA CGTGGTCAAA TCAAAGTWGG 420
 TGAAGAAGTT GAAATCATCG GTATGCACGA AACTTCTAAA ACAACTGTTA CTGGTGTAGA 480
 AATGTTCCGT AAATTATTAG ACTACGCTGA AGCTGGTGAC AACATCGGTG CTTTATTACG 540
 TGGTGTGCA CGTGAAGACG TACAACGTGG TCAAGTATTA GCTGCTCCTG GTTCTATTAC 600
 ACCACACACA AAATTCAAAG CTGAAGTATA CGTATTATCT AAAGATGAAG GTGGACGTCA 660
 CACTCCATTC TTCCTAACT ATCGCCACACA ATTCTATTTT CRTACTACTG ACGTAACTGG 720
 TGTGTGAAAC TTACCAGAAG GTACAGAAAT GGTATGCCT GGCGACAACG TTGAAATGAC 780
 AGTTGAATTA ATCGCTCCAA TCGCTATCGA AGAC 814

(2) INFORMATION FOR SEQ ID NO: 142:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus saprophyticus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

| | |
|---|-----|
| CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACACAT | 60 |
| TCTTTTATCA CGTRACGTTG GTGYTCCAGC ATTAGTTGTA TTCTTAAACA AAGTTGACAT | 120 |
| GGTTGACGAY GAAGAATTAT TAGAATTRGT AGAAATGGAA GTTCGTGRCT TATTAAGCGA | 180 |
| ATATGACTTC CCAGGTGACG ATGTACCTGT AATCTCTGGT TCTGCATTAA AAGCTTTAGA | 240 |
| AGGCGACGCT GACTATGAGC AAAAAATCTT AGACTTAATG CAAGCTGTTG ATGACTYCAT | 300 |
| TCCAACACCA GAACGTGATT CTGACAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC | 360 |
| AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTGAA CGTGGTCAAA TCAAAGTCGG | 420 |
| TGAAGAAATC GARATCATCG GTATGCAAGA AGAATCAAGC AAAACAACTG TTACTGGTGT | 480 |
| AGAAATGTTC CGTAAATTAT TAGACTACGC TGAAGCTGGT GACAACATTG GTGCATTATT | 540 |
| ACGTGGTGTT TCACGTGATG ATGTACAACG TGGTCAAGTT TTAGCTGCTC CTGGTACTAT | 600 |
| CACACCACAT ACAAATTC AAGCGGATGT TTACGTTTTA TCTAAAGATG AAGGTGGTCG | 660 |
| TCATACGCCA TTCTTCACTA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC | 720 |
| TGGTGTGTT AACTTACCAG AAGGTACTGA AATGGTTATG CCTGGCGATA ACGTTGAAAT | 780 |
| GGATGTTGAA TTAATTTCTC CAATCGCTAT TGAAGAC | 817 |

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 817 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Staphylococcus simulans*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

| | |
|---|-----|
| CGGCGGTATC TTAGTAGTAT CTGCTGCAGA TGGTCCAATG CCACAAACTC GTGAACACAT | 60 |
| CTTATTATCA CGTAACGTTG GTGTACCAGC TTTAGTTGTA TTCTTAAACA AAGCTGACAT | 120 |
| GGTTGACGAC GAAGAATTAT TAGAATTAGT TGAAATGGAA GTTCGTGACT TATTATCTGA | 180 |

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| | |
|---|-----|
| ATACGACTTC CCTGGTGACG ATGTACCAGT TATCGTTGGT TCTGCATTAA AAGCTTTAGA | 240 |
| AGGCGACCCA GAATACGAAC AAAAAATCTT AGACTTAATG CAAGCTGTAG ATGACTACAT | 300 |
| CCCAACTCCA GAACGTGACT CTGATAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC | 360 |
| AATCACTGGT CGTGGTACTG TAGCAACAGG CCGTGTGAA CGTGGTCAAA TCAAAGTCGG | 420 |
| TGAAGAAGTT GAAATCATCG GTATCACTGA AGAAAGCAAG AAAACAACAG TTACAGGTGT | 480 |
| AGAAATGTTT CGTAAATTAT TAGACTACGC TGAAGCTGGT GACAACATCG GTGCTTTATT | 540 |
| ACGTGGTGTT GCACGTGAAG ACGTACAACG TGGACAAGTA TTAGCAGCTC CTGGCTCTAT | 600 |
| TACTCCACAC ACAAATTC AAGCTGATGT TTACGTTT TCTAAAGAAG AAGGTGGACG | 660 |
| TCATACTCCA TTCTTCACTA ACTACCGCCC ACAATTCTAC TTCCGTACTA CTGACGTAAC | 720 |
| TGGCGTTGTT CACTTACCAG AAGGTACTGA AATGGTTATG CCTGGCGATA ACGTAGAAAT | 780 |
| GACTGTTGAA TTGATCGCTC CAATCGCGAT TGAAGAC | 817 |

(2) INFORMATION FOR SEQ ID NO: 144:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus agalactiae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

| | |
|---|-----|
| CGGAGCTATC CTTGTAGTTG CTTCAACTGA TGGACCAATG CCACAACTC GTGAGCACAT | 60 |
| CCTTCTTTCA CGTCAAGTTG GTGTTAAACA CCTTATCGTA TTCATGAACA AAGTTGACCT | 120 |
| TGTTGATGAT GAAGAATTGC TTGAATTGGT TGAAATGGAA ATTCGTGACC TTCTTTCAGA | 180 |
| ATACGACTTC CCAGGTGATG ACCTTCCAGT TATCCAAGGT TCAGCTCTTA AAGCACTTGA | 240 |
| AGGCGACGAA AAATACGAAG ACATCATCAT GGAATTGATG AGCACTGTTG ATGAGTACAT | 300 |
| TCCAGAACCA GAACGTGATA CTGACAAACC TTTACTTCTT CCAGTTGAAG ATGTATTCTC | 360 |
| AATCACTGGA CGTGGTACAG TTGCTTCAGG ACGTATCGAC CGTGGTACTG TTCGTGTCAA | 420 |
| CGACGAAGTT GAAATCGTTG GTATTAAAGA AGATATCCAA AAAGCAGTTG TTACTGGTGT | 480 |
| TGAAATGTTT CGTAAACAAC TTGACGAAGG TCTTGACGGG GACAACGTTG GTGTTCTTCT | 540 |
| TCGTGGTGTT CAACGTGATG AAATCGAAGC TGGTCAAGTT CTTGCTAAAC CAGGTTCAAT | 600 |

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CAACCCACAC ACTAAATTTA AAGGTGAAGT TTACATCCTT TCTAAAGAAG AAGGTGGACG 660
 TCATACTCCA TTCTTCAACA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC 720
 AGGTTCAATC GAACTTCCAG CAGGAACAGA AATGGTTATG CCTGGTGATA ACGTTACTAT 780
 CGAAGTTGAA TTGATTCACC CAATCGCCGT AGAACAA 817

(2) INFORMATION FOR SEQ ID NO: 145:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pneumoniae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

CGGAGCTATC CTTGTAGTAG CTTCAACTGA CGGACCAATG CCACAAACTC GTGAGCACAT 60
 CCTTCTTTCA CGTCAGGTTG GTGTTAAACA CCTTATCGTC TTCATGAACA AAGTTGACTT 120
 GGTTGACGAC GAAGAATTGC TTGAATTGGT TGAAATGGAA ATCCGTGACC TATTGTCAGA 180
 ATACGACTTC CCAGGTGACG ATCTTCCAGT TATCCAAGGT TCAGCACTTA AAGCTCTTGA 240
 AGGTGACTCT AAATACGAAG ACATCGTTAT GGAATTGATG AACACAGTTG ATGAGTATAT 300
 CCCAGAACCA GAACGTGACA CTGACAAACC ATTGCTTCTT CCAGTCGAGG ACGTATTCTC 360
 AATCACTGGA CGTGGTACAG TTGCTTCAGG ACGTATCGAC CGTGGTATCG TTAAAGTCAA 420
 CGACGAAATC GAAATCGTTG GTATCAAAGA AGAAACTCRA AAAGCAGTTG TTAGTGGTGT 480
 TGAAATGTTC CGTAAACAAC TTGACGAAGG TCTTGCTGGA GATAACGTAG GTGTCCTTCT 540
 TCGTGGTGTT CAACGTGATG AAATCGAACG TGGACAAGTT ATCGCTAAAC CAGGTTCAAT 600
 CAACCCACAC ACTAAATTCA AAGGTGAAGT CTACATCCTT ACTAAAGAAG AAGGTGGACG 660
 TCACACTCCA TTCTTCAACA ACTACCGTCC ACAATTCTAC TTCCGTACTA CTGACGTTAC 720
 AGGTTCAATC GAACTTCCAG CAGGTACTGA AATGGTAATG CCTGGTGATA ACGTGACAA 780
 CGACGTTGAG TTGATTCACC CAATCGCCGT AGAACAA 817

(2) INFORMATION FOR SEQ ID NO: 146:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 817 base pairs
- (B) TYPE: nucleic acid

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- (C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Streptococcus salivarius*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

| | |
|---|-----|
| CGGTGCGATC CTTGTAGTAG CATCTACTGA CGGACCAATG CCACAAACTC GTGAGCACAT | 60 |
| CCTTCTTTCA CGTCAGGTTG GTGTTAAACA CCTTATCGTC TTCATGAACA AAGTTGACTT | 120 |
| GGTTGACGAT GAAGAATTGC TTGAATTGGT TGAAATGGAA ATCCGTGACC TTCTTTCAGA | 180 |
| ATACGATTTC CCAGGTGATG ACATTCCAGT TATCCAAGGT TCAGCTCTTA AAGCTCTTGA | 240 |
| AGGTGATTCT AAATACGAAG ACATCATCAT GGAATTGATG AACACTGTTG ACGAATACAT | 300 |
| CCCAGAACCA GAACGTGACA CTGACAAACC ATTGTTGCTT CCAGTCGAAG ACGTATTCTC | 360 |
| AATCACTGGT CGTGGTACTG TTGCTTCAGG ACGTATCGAC CGTGGTGTG TTCGTGTCAA | 420 |
| TGACGAAGTT GAAATCGTTG GTCTTAAAGA AGACATCCAA AAAGCAGTTG TTAAGTGGTG | 480 |
| TGAAATGTTC CGTAAACAAC TTGACGRAGG TATTGCCGGA GATAACGTCG GTGTTCTTCT | 540 |
| TCGTGGTATC CAACGTGATG AAATCGAACG TGGTCAAGTA TTGGCTGCAC CTGGTTCAAT | 600 |
| CAACCCACAC ACTAAATTCA AAGGTGAAGT TTACATCCTT TCTAAAGAAG AAGGTGGACG | 660 |
| TCACACTCCA TTCTTCAACA ACTACCGTCC ACAGTTCTAC TTCCGTACAA CTGACGTAAC | 720 |
| AGGTTCAATC GAACTTCCTG CAGGTACTGA AATGGTTATG CCTGGTGATA ACGTGACTAT | 780 |
| CGACGTTGAG TTGATCCACC CAATCGCCGT TGAACAA | 817 |

(2) INFORMATION FOR SEQ ID NO: 147:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 897 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Agrobacterium tumefaciens*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

| | |
|---|-----|
| AACATGATCA CCGGTGCTGC CGAGATGGAC GGCGCGATCC TGGTTTGCTC GGCTGCCGAC | 60 |
| GGCCCGATGC CACAGACCCG CGAGCACATC CTGCTTGCCC GTCAGGTGGG CGTTCCGGCC | 120 |

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ATCGTCGTGT TCCTCAACAA GGTGACGACG GTTGACGACG CCGAGCTTCT CGAGCTCGTC 180
 GAGCTTGAAG TTCGCGAACT TCTGTCGTCC TACGACTTCC CGGGCGACGA TATCCCGATC 240
 ATCAAGGGTT CGGCACTTGC TGCTCTTGAA GATTCTGACA AGAAGATCGG TGAAGACGCG 300
 ATCCGCGAGC TGATGGCTGC TGTCGACGCC TACATCCCGA CGCCTGAGCG TCCGATCGAC 360
 CAGCCGTTCC TGATGCCGAT CGAAGACGTG TTCTCGATCT CGGGTCGTGG TACGGTTGTG 420
 ACGGGTCGCG TTGAGCGCGG TATCGTCAAG GTTGGTGAAG AAGTCGAAAT CGTCGGCATC 480
 CGTCCGACCT CGAAGACGAC TGTTACCGGC GTTGAAATGT TCCGCAAGCT GCTCGACCAG 540
 GGCCAGGCCG GCGACAACAT CGGTGCACTC GTTCGCGGCG TTACCCGTGA CGGCGTCGAG 600
 CGTGGTCAGA TCCTGTGCAA GCCGGGTTTC GTCAAGCCGC ACAAGAAGTT CATGGCAGAA 660
 GCCTACATCC TGACGAAGGA AGAAGCGGCG CGTCATACGC CGTTCTTCAC GAACTACCGT 720
 CCGCAGTTCT ACTTCCGTAC GACTGACGTT ACCGGTATCG TTTGCTTCC TGAAGGCACG 780
 GAAATGGTTA TGCCTGGCGA CAACGTCCT GTTGAAGTCG AGCTGATCGT TCCGATCGCG 840
 ATGGAAGAAA AGCTGCGCTT CGCTATCCGC GAAGGCGGCC GTACCGTCGG CGCCGGC 897

(2) INFORMATION FOR SEQ ID NO: 148:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 885 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Bacillus subtilis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

ATGATCACTG GTGCTGCGCA AATGGACGGA GCTATCCTTG TAGTATCTGC TGCTGATGGC 60
 CCAATGCCAC AAACCTCGTGA GCACATCCTT CTTTCTAAAA ACGTTGGTGT ACCATACATC 120
 GTTGTATTCT TAAACAAATG CGACATGGTA GACGACGAAG AGCTTCTTGA ACTAGTTGAA 180
 ATGGAAGTTC GCGATCTTCT TAGCGAATAC GACTTCCCTG GTGATGATGT ACCAGTTGTT 240
 AAAGGTTCTG CTCTTAAAGC TCTTGAAGGA GACGCTGAGT GGAAGCTAA AATCTTCGAA 300
 CTTATGGATG CGGTTGATGA GTACATCCCA ACTCCAGAAC GCGACACTGA AAAACCATTC 360
 ATGATGCCAG TTGAGGACGT ATTCTCAATC ACTGGTCGTG GTACAGTTGC TACTGGCCGT 420
 GTAGAACGCG GACAAGTTAA AGTCGGTGAC GAAGTTGAAA TCATCGGTCT TCAAGAAGAG 480

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AACAAGAAAA CAACTGTTAC AGGTGTTGAA ATGTTCCGTA AGCTTCTTGA TTACGCTGAA 540
 GCTGGTGACA ACATTGGTGC CCTTCTTCGC GGTGTATCTC GTGAAGAAAT CCAACGTGGT 600
 CAAGTACTTG CTAAACCAGG TACAATCACT CCACACAGCA AATTCAAAGC TGAAGTTTAC 660
 GTTCTTTCTA AAGAAGAGGG TGGACGTCAT ACTCCATTCT TCTCTAACTA CCGTCCTCAG 720
 TTCTACTTCC GTACAACTGA CGTAACTGGT ATCATCCATC TTCCAGAAGG CGTAGAAATG 780
 GTTATGCCTG GAGATAACAC TGAAATGAAC GTTGAACCTA TTTCTACAAT CGCTATCGAA 840
 GAAGGAACTC GTTTCTCTAT TCGTGAAGGC GGACGTACTG TTGGT 885

(2) INFORMATION FOR SEQ ID NO: 149:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 882 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Bacteroides fragilis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

ATGGTTACTG GTGCTGCTCA GATGGACGGT GCTATCATTG TAGTTGCTGC TACTGATGGT 60
 CCGATGCCTC AGACTCGTGA GCACATCCTT TTGGCTCGTC AGGTAAACGT TCCGAAGCTG 120
 GTTGTATTCA TGAACAAGTG CGATATGGTT GAAGATGCTG AGATGTTGGA ACTTGTTGAA 180
 ATGGAATGA GAGAATTGCT TTCATTCTAT GATTTGACG GTGACAATAC TCCGATCATT 240
 CAGGGTTCTG CTCTTGGTGC ATTGAACGGC GTAGAAAAAT GGGAAGACAA AGTAATGGAA 300
 CTGATGGAAG CTGTTGATAC TTGGATTCCA CTGCCTCCGC GCGATGTTGA TAAACCTTTC 360
 TTGATGCCGG TAGAAGACGT GTTCTCTATC ACAGGTCGTG GTACTGTAGC TACAGGTCGT 420
 ATCGAAACTG GTGTTATCCA TGTAGGTGAT GAAATCGAAA TCCTCGGTTT GGGTGAAGAT 480
 AAGAAATCAG TTGTAACAGG TGTGAAATG TTCCGCAAAC TTCTGGATCA GGGTGAAGCT 540
 GGTGACAACG TAGGTCTGTT GCTTCGTGGT GTTGACAAGA ACGAAATCAA ACGTGGTATG 600
 GTTCTTTGTA AACCGGGTCA GATTAAACCT CACTCTAAAT TCAAAGCAGA GGTTTATATC 660
 CTGAAGAAAG AAGAAGGTGG TCGTCACACT CCATTCCATA ACAAATATCG TCCTCAGTTC 720
 TACCTGCGTA CTATGGACTG TACAGGTGAA ATCACTCTTC CGGAAGGAAC TGAAATGGTA 780
 ATGCCGGGTG ATAACGTAAC TATCACTGTA GAGTTGATCT ATCCGGTTGC ACTGAACATC 840

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GGTCTTCGTT TCGCTATCCG CGAAGGTGGA CGTACAGTAG GT

882

(2) INFORMATION FOR SEQ ID NO: 150:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 888 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Borrelia burgdorferi*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

| | |
|--|-----|
| AATATGATTA CAGGAGCAGC TCAAATGGAT GCAGCGATAC TTTTAGTTGC TGCTGATAGT | 60 |
| GGTGCTGAGC CTCAAACAAA AGAGCATTTC CTTCTTGCTC AAAGAATGGG AATAAAGAAA | 120 |
| ATAATAGTTT TTTTAAATAA ATTGGACTTA GCAGATCCTG AACTTGTTGA GCTTGTTGAA | 180 |
| GTTGAAGTTT TAGAACTTGT TGAAAAATAT GGCTTTTCAG CTGATACTCC AATAATCAAA | 240 |
| GGTTCAGCTT TTGGGGCTAT GTCAAATCCA GAAGATCCTG AATCTACAAA ATGCGTTAAA | 300 |
| GAACTTCTTG AATCTATGGA TAATTATTTT GATCTTCCAG AAAGAGATAT TGACAAGCCA | 360 |
| TTTTTGCTTG CTGTTGAAGA TGTATTTTCT ATTTTCAGGAA GAGGCACTGT TGCTACTGGG | 420 |
| CGTATTGAAA GAGGTATTAT TAAAGTTGGT CAAGAAGTTG AAATAGTTGG AATTAAAGAA | 480 |
| ACCAGAAAAA CTA CTGTTAC TGGTGTGAA ATGTTCCAGA AAATCTTGA GCAAGGTCAA | 540 |
| GCAGGGGATA ATGTTGGTCT TCTTTTGAGA GGC GTTGATA AAAAAGACAT TGAGAGGGGG | 600 |
| CAAGTTTGT CAGCTCCAGG TACAATTACT CCACACAAGA AATTTAAAGC TTCAATTTAT | 660 |
| TGTTTGACTA AAGAAGAAGG CGGTAGGCAC AAGCCATTTT TCCCAGGTA TAGACCACAG | 720 |
| TTCTTTTSTA GAACAACCGA TGTTACTGGA GTTGTGCTT TAGAGGGCAA AGAAATGGTT | 780 |
| ATGCCTGGTG ATAATGTTGA TATTATTGTT GAGCTGATCT CTTCAATAGC TATGGATAAG | 840 |
| AATGTAGAAT TTGCTGTTTCG AGAAGGTGGA AGAACCGTTG CTT CAGGA | 888 |

(2) INFORMATION FOR SEQ ID NO: 151:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Brevibacterium linens*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

```

AACATGATCA CCGGTGCCGC TCAGATGGAC GGTGCGATCC TCGTCGTCGC CGCTACCGAC      60
GGACCGATGC CCCAGACCCG TGAGCACGTG CTGCTCGCGC GTCAGGTCGG CGTTCCCTAC      120
ATCGTCGTGG CTCTGAACAA GTCCGACATG GTCGATGACG AGGAGCTCCT CGAGCTCGTC      180
GAATTCGAGG TCCGCGACCT GCTCTCGAGC CAGGACTTCG ACGGAGACAA CGTCCGGTC      240
ATTCCGGTGT CCGCTCTCAA GGCGCTGGAA GGCGACGAGA AGTGGGTCAA GAGCGTTCAG      300
GATCTCATGG CTGCCGTCGA TGACAACGTT CCGGAGCCGG AGCGCGATGT CGACAAGCCG      360
TTCCTCATGC CCGTCGAGGA CGTCTTCACG ATCACCGGTC GTGGAACCGT CGTCACCGGT      420
CGTGTCGAGC GCGGCGTGCT CCTGCCTAAC GACGAAATCG AAATCGTCGG CATCAAGGAG      480
AAGTCGTCCA AGACGACTGT CACCGCTATC GAGATGTTCC GCAAGACCCT GCCGGATGCC      540
CGTGCAGGTG AGAACGTCGG TCTGCTCCTC CGCGGCACCA AGCGCGAGGA TGTGAGCGC      600
GGTCAGGTCA TCGTGAAGCC GGGTTCGATC ACCCGCACA CCAAGTTCGA GGTCAGGTC      660
TACATCCTGA GCAAGGACGA GGGCGGACGT CACAACCCGT TCTACTCGAA CTACCGTCCG      720
CAGTTCTACT TCCGGACCAC GGACGTCACC GGTGTCATCA CGCTGCCCCA GGGCACCGAG      780
ATGGTCATGC CCGGCGACAA CACCGATATG TCGGTCGAGC TCATCCAGCC GATCGCTATG      840
GAGGACCGCC TCCGCTTCGC AATCCGCGAA GGTGGCCGCA CCGTCGGCGC CGGT      894

```

(2) INFORMATION FOR SEQ ID NO: 152:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 888 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Burkholderia cepacia*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

```

ATGATCACGG GCGCAGCGCA GATGGACGGC GCGATCCTGG TTTGCTCGGC AGCAGACGGC      60
CCGATGCCGC AAACGCGTGA GCACATCCTG CTGGCGCGTC AGGTTGGTGT TCCGTACATC      120
ATCGTGTTC TGAACAAGTG CGACAGTGTG GACGACGCTG AACTGCTCGA GCTGGTTCGAG      180

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ATGGAAGTTC GCGAACTCCT GTCGAAGTAC GACTTCCCGG GCGACGACAC GCCGATCGTG 240
 AAGGGTTCCG CCAAGCTGGC GCTGGAAGGC GACACGGGCG AGCTGGGCGA AGTGGCGATC 300
 ATGAGCCTGG CAGACGCGCT GGACACGTAC ATCCCACGCG CGGAGCGTGC AGTTGACGGC 360
 GCGTTCCTGA TGCCGGTGA AGACGTGTTT TCGATCTCGG GCCGTGGTAC GGTGGTGACG 420
 GGTCGTGTGC AGCGCGGCAT CGTGAAGGTC GGCGAAGAAA TCGAAATCGT CGGTATCAAG 480
 CCGACGGTGA AGACGACCTG CACGGGCGTT GAAATGTTCC GCAAGCTGCT GGACCAAGGT 540
 CAGGCAGGCG ACAACGTCGG TATCCTGCTG CGCGGCACGA AGCGTGAAGA CGTGGAGCGT 600
 GGCCAGGTTC TGGCGAAGCC GGGTTCGATC ACGCCGCACA CGCACTTCAC GGCTGAAGTG 660
 TACGTGCTGA GCAAGGACGA AGGCGGCCGT CACACGCCGT TCTTCAACAA CTACCGTCCG 720
 CAGTTCTACT TCCGTACGAC GGACGTGACG GGCTCGATCG AGCTGCCGAA GGACAAGGAA 780
 ATGGTGATGC CGGGCGACAA CGTGTCGATC ACGGTGAAGC TGATTGCTCC GATCGCGATG 840
 GAAGAAGGTC TGCGCTTCGC AATCCGTGAA GGCGGCCGTA CGGTCCGC 888

(2) INFORMATION FOR SEQ ID NO: 153:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Chlamydia trachomatis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

AACATGATCA CCGGTGCGGC TCAAATGGAC GGGGCTATTC TAGTAGTTTC TGCAACAGAC 60
 GGAGCTATGC CTCAACTAA AGAGCATATT CTTTGGCAA GACAAGTTGG GGTTCCTTAC 120
 ATCGTTGTTT TTCTCAATAA AATTGACATG ATTTCCGAAG AAGACGCTGA ATTGGTCGAC 180
 TTGGTTGAGA TGGAGTTGGC TGAGCTTCTT GAAGAGAAAG GATACAAAGG GTGTCCAATC 240
 ATCAGAGGTT CTGCTCTGAA AGCTTTGGAA GGAGATGCTG CATACATAGA GAAAGTTCGA 300
 GAGCTAATGC AAGCCGTCGA TGATAATATC CCTACTCCAG AAAGAGAAAT TGACAAGCCT 360
 TTCTTAATGC CTATTGAGGA CGTGTTCTCT ATCTCCGGAC GAGGAACTGT AGTAACTGGA 420
 CGTATTGAGC GTGGAATTGT TAAAGTTTCC GATAAAGTTC AGTTGGTCGG TCTTAGAGAT 480
 ACTAAAGAAA CGATTGTTAC TGGGGTTGAA ATGTTAGAA AAGAACTCCC AGAAGGTCGT 540

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| | |
|---|-----|
| GCAGGAGAGA ACGTTGGATT GCTCCTCAGA GGTATTGGTA AGAACGATGT GGAAAGAGGA | 600 |
| ATGGTTGTTT GCTTGCCAAA CAGTGTTAAA CCTCATACAC AGTTTAAGTG TGCTGTTTAC | 660 |
| GTTCTGCAAA AAGAAGAAGG TGGACGACAT AAGCCTTTCT TCACAGGATA TAGACCTCAA | 720 |
| TTCTTCTTCC GTACAACAGA CGTTACAGGT GTGGTAACTC TGCCTGAGGG AGTTGAGATG | 780 |
| GTCATGCCTG GGGATAACGT TGAGTTTGAA GTGCAATTGA TTAGCCCTGT GGCTTTAGAA | 840 |
| GAAGGTATGA GATTGCGAT TCGTGAAGGT GGTCGTACAA TCGGTGCTGG A | 891 |

(2) INFORMATION FOR SEQ ID NO: 154:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Escherichia coli*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

| | |
|--|-----|
| AACATGATCA CCGTGCTGC GCAGATGGAC GGC GCGATCC TGGTAGTTGC TGCGACTGAC | 60 |
| GGCCCGATGC CGCAGACTCG TGAGCACATC CTGCTGGGTC GTCAGGTAGG CGTTCCGTAC | 120 |
| ATCATCGTGT TCCTGAACAA ATGCGACATG GTTGATGACG AAGAGCTGCT GGAAGTGGTT | 180 |
| GAAATGGAAG TTCGTGAACT TCTGTCTCAG TACGACTTCC CGGGCGACGA CACTCCGATC | 240 |
| GTTCTGTGGT CTGCTCTGAA AGCGCTGGAA GGC GACGACG AGTGGGAAGC GAAAATCCTG | 300 |
| GAACTGGCTG GCTTCTGGA TTCTTACATT CCGGAACCAG AGCGTGCGAT TGACAAGCCG | 360 |
| TTCTGCTGCG CGATCGAAGA CGTATTCTCC ATCTCCGGTC GTGGTACCGT TGTTACCGGT | 420 |
| CGTGTAGAAC GCGGTATCAT CAAAGTTGGT GAAGAAGTTG AAATCGTTGG TATCAAAGAG | 480 |
| ACTCAGAACT CTACCTGTAC TGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGCCGT | 540 |
| GCTGGTGAGA ACGTAGGTGT TCTGCTGCGT GGTATCAAAC GTGAAGAAAT CGAACGTGGT | 600 |
| CAGGTACTGG CTAAGCCGGG CACCATCAAG CCGCACACCA AGTTCGAATC TGAAGTGATC | 660 |
| ATTCTGTCCA AAGATGAAGG CGGCCGTCAT ACTCCGTTCT TCAAAGGCTA CCGTCCGCAG | 720 |
| TTCTACTTCC GTACTACTGA CGTGACTGGT ACCATCGAAC TGCCGGAAGG CGTAGAGATG | 780 |
| GTAATGCCGG GCGACAACAT CAAAATGGTT GTTACCCTGA TCCACCCGAT CGCGATGGAC | 840 |
| GACGGTCTGC GTTTCGCAAT CCGTGAAGGC GGCCGTACCG TTGGCGCGGG C | 891 |

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(2) INFORMATION FOR SEQ ID NO: 155:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Fibrobacter succinogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

```

AACATGGTGA CTGGTGCTGC TCAGATGGAC GGCCTATCC TCGTTGTTGC CGCTACTGAC      60
GGTCCGATGC CGCAGACTCG CGAACACATC CTTCTCGCTC ACCAGGTTGG CGTGCCGAAG      120
ATCGTCGTGT TCATGAACAA GTGCGACATG GTTGACGATG CTGAAATTCT CGACCTCGTC      180
GAAATGGAAG TTCGCGAACT CCTCTCCAAG TATGACTTCG ACGGTGACAA CACCCCGATC      240
ATCCGTGGTT CCGCTCTCAA GGCCCTCGAA GCGGATCCGG AATACCAGGA CAAGGTCATG      300
GAACTCATGA ACGCTTGCGA CGAATACATC CCGCTCCCGC AGCGCGATAC CGACAAGCCG      360
TTCCTCATGC CGATCGAAGA CGTGTTACAG ATTACTGGCC GCGGCACTGT CGCTACTGGC      420
CGTATCGAAC GCGGTGTCGT TCGCTTGAAC GACAAGGTTG AACGTATCGG TCTCGGTGAA      480
ACCACCGAAT ACGTCATCAC CGGTGTTGAA ATGTTCCGTA AGCTCCTCGA CGACGCTCAG      540
GCAGGTGACA ACGTTGGTCT CCTCCTCCGT GGTGCTGAAA AGAAGGACAT CGTCCGTGGC      600
ATGGTTCTCG CAGCTCCGAA GTCTGTCACT CCGCACACCG AATTTAAGGC TGAAATCTAC      660
GTTCTCACGA AGGACGAAGG TGGCCGTCAC ACGCCGTTCA TGAATGGCTA CCGTCCGCAG      720
TTCTACTTCC GCACCACCGA CGTTACTGGT ACGATCCAGC TCCCGGAAGG TGTCGAAATG      780
GTTACTCCGG GTGACACGGT CACGATCCAC GTGAACCTCA TCGCTCCGAT CGCTATGGAA      840
AAGCAGCTCC GCTTCGCTAT CCGTGAAGGT GGACGTACTG TTGGTGCTGG C              891

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(2) INFORMATION FOR SEQ ID NO: 156:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Flavobacterium ferrugineum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

| | |
|---|-----|
| AACATGATCA CCGGTGCTGC CCAGATGGAC GGTGCTATCT TAGTTGTGGC TGCATCAGAC | 60 |
| GGTCCTATGC CTCAAACAAA AGAACACATC CTGCTTGCTG CCCAGGTAGG TGTACCTAAA | 120 |
| ATGGTTGTGT TTCTGAATAA AGTTGACCTC GTTGACGACG AAGAGCTCCT GGAGCTGGTT | 180 |
| GAGATCGAGG TTCGCGAAGA ACTGACTAAA CGCGGTTTCG ACGGCGACAA CACTCCAATC | 240 |
| ATCAAAGGTT CCGCTACAGG CGCCCTCGCT GGTGAAGAAA AGTGGGTAA AGAAATTGAA | 300 |
| AACCTGATGG ACGCTGTTGA CAGCTACATC CCACTGCCTC CTCGTCCGGT TGATCTGCCG | 360 |
| TTCCTGATGA GCGTAGAGGA CGTATTCTCT ATCACTGGTC GTGGTACTGT TGCTACCGGT | 420 |
| CGTATCGAGC GTGGCCGTAT CAAAGTTGGT GAGCCTGTTG AGATCGTAGG TCTGCAGGAG | 480 |
| TCTCCCTGA ACTCTACCGT TACAGGTGTT GAGATGTTCC GCAAACCTCT CGACGAAGGT | 540 |
| GAAGCTGGTG ATAACGCCGG TCTCCTCCTC CGTGGTGTG AAAAAACACA GATCCGTCGC | 600 |
| GGTATGGTAA TCGTTAAACC CGGTTCCATC ACTCCGCACA CGGACTTCAA AGGCGAAGTT | 660 |
| TACGTAATGA GCAAAGACGA AGGTGGCCGT CACACTCCAT TCTTCAACAA ATACCGTCCT | 720 |
| CAATCTACT TCCGTACAAC TGACGTTACA GGTGAAGTAG AACTGAACGC AGGAACAGAA | 780 |
| ATGGTTATGC CTGGTGATAA CACCAACCTG ACCGTTAAAC TGATCCAACC GATCGCTATG | 840 |
| GAAAAAGGTC TGAAATTCGC GATCCGCGAA GGTGGCCGTA CCGTAGGTGC AGGA | 894 |

(2) INFORMATION FOR SEQ ID NO: 157:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Haemophilus influenzae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

| | |
|---|-----|
| AATATGATTA CTGGTGCGGC ACAAATGGAT GGTGCTATTT TAGTAGTAGC AGCAACAGAT | 60 |
| GGTCCTATGC CACAACTCG TGAACACATC TTATTAGGTC GCCAAGTAGG TGTTCCATAC | 120 |
| ATCATCGTAT TCTTAAACAA ATGCGACATG GTAGATGACG AAGAGTTATT AGAATTAGTC | 180 |
| GAAATGGAAG TTCGTGAACT TCTATCTCAA TATGACTTCC CAGGTGACGA TACACCAATC | 240 |

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| | |
|---|-----|
| GTACGTGGTT CAGCATTACA AGCGTTAAAC GGCGTAGCAG AATGGGAAGA AAAAATCCTT | 300 |
| GAGTTAGCAA ACCACTTAGA TACTTACATC CCAGAACCAG AACGTGCGAT TGACCAACCG | 360 |
| TTCCTTCTTC CAATCGAAGA TGTGTTCTCA ATCTCAGGTC GTGGTACTGT AGTAACAGGT | 420 |
| CGTGTAGAAC GAGGTATTAT CCGTACAGGT GATGAAGTAG AAATCGTCGG TATCAAAGAT | 480 |
| ACAGCGAAAA CTACTGTAAC GGGTGTGAA ATGTTCCGTA AATTACTTGA CGAAGGTCGT | 540 |
| GCAGGTGAAA ACATCGGTGC ATTATTACGT GGTACCAAAC GTGAAGAAAT CGAACGTGGT | 600 |
| CAAGTATTAG CGAAACCAGG TTCAATCACA CCACACACTG ACTTCGAATC AGAAGTGATC | 660 |
| GTATTATCAA AAGATGAAGG TGGTCGTCAT ACTCCATTCT TCAAAGGTTA CCGTCCACAA | 720 |
| TTCTATTTCC GTACAACAGA CGTGACTGGT ACAATCGAAT TACCAGAAGG CGTGGAATG | 780 |
| GTAATGCCAG GCGATAACAT CAAGATGACA GTAAGCTTAA TCCACCCAAT TGCGATGGAT | 840 |
| CAAGGTTTAC GTTTCGCAAT CCGTGAAGGT GGCCGTACAG TAGGTGCAGG C | 891 |

(2) INFORMATION FOR SEQ ID NO: 158:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 906 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Helicobacter pylori*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

| | |
|--|-----|
| AACATGATCA CCGGTGCGGC GCAAATGGAC GGAGCGATTT TGGTTGTTTC TGCAGCTGAT | 60 |
| GGCCCTATGC CTCAAAC TAG GGAGCATATC TTATTGTCTC GTCAAGTAGG CGTGCCTCAC | 120 |
| ATCGTTGTTT TCTTAAACAA ACAAGACATG GTAGATGACC AAGAATTGTT AGAACTTGTA | 180 |
| GAAATGGAAG TGCGCGAATT GTTGAGCGCG TATGAATTTT CTGGCGATGA CACTCCTATC | 240 |
| GTAGCGGGTT CAGCTTTAAG AGCTTTAGAA GAAGCAAAGG CTGGTAATGT GGGTGAATGG | 300 |
| GGTGAAAAAG TGCTTAAACT TATGGCTGAA GTGGATGCCT ATATCCCTAC TCCAGAAAGA | 360 |
| GACACTGAAA AAACCTTCTT GATGCCGGTT GAAGATGTGT TCTCTATTGC GGGTAGAGGG | 420 |
| ACTGTGGTTA CAGGTAGGAT TGAAAGAGGC GTGGTGAAAG TAGGCGATGA AGTGGAATC | 480 |
| GTTGGTATCA GACCTACACA AAAAACGACT GTAACCGGTG TAGAAATGTT TAGGAAAGAG | 540 |
| TTGGA AAAAG GTGAAGCCGG CGATAATGTG GCGTGCTTT TGAGAGGAAC TAAAAAGAA | 600 |

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| | |
|---|-----|
| GAAGTGAAC GCGGTATGGT TCTATGCAAA CCAGGTTCTA TCACTCCGCA CAAGAAATTT | 660 |
| GAGGGAGAAA TTTATGTCCT TTCTAAAGAA GAAGGCGGGA GACACACTCC ATTCTTCACC | 720 |
| AATTACCGCC CGCAATTCTA TGTGCGCACA ACTGATGTGA CTGGCTCTAT CACCCTTCCT | 780 |
| GAAGGCGTAG AAATGGTTAT GCCTGGCGAT AATGTGAAAA TCACTGTAGA GTTGATTAGC | 840 |
| CCTGTTGCGT TAGAGTTGGG AACTAAATTT GCGATTCTGT AAGGCGGTAG GACCGTTGGT | 900 |
| GCTGGT | 906 |

(2) INFORMATION FOR SEQ ID NO: 159:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Micrococcus luteus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

| | |
|--|-----|
| AACATGATCA CCGGCGCCGC TCAGATGGAC GGCGCGATCC TCGTGGTCGC CGCTACCGAC | 60 |
| GGCCCCGATGG CCCAGACCCG TGAGCACGTG CTCCTGGCCC GCCAGGTCGG CGTGCCGGCC | 120 |
| CTGCTCGTGG CCCTGAACAA GTCGGACATG GTGGAGGACG AGGAGCTCCT CGAGCGTGTC | 180 |
| GAGATGGAGG TCCGGCAGCT GCTGTCCTCC AGGAGCTTCG ACGTCGACGA GGCCCCGGTC | 240 |
| ATCCGCACCT CCGCTCTGAA GGCCCTCGAG GGCGACCCC AGTGGGTCAA GTCCGTCGAG | 300 |
| GACCTCATGG ATGCCGTGGA CGAGTACATC CCGGACCCGG TGC GCGACAA GGACAAGCCG | 360 |
| TTCTTGATGC CGATCGAGGA CGTCTTCACG ATCACC GGCC GTGGCACC GTTGACCGGT | 420 |
| CGCGCCGAGC GCGGCACCC T GAAGATCAAC TCCGAGGTCG AGATCGTCGG CATCCGCGAC | 480 |
| GTGCAGAAGA CCACTGTCAC CGGCATCGAG ATGTTCCACA AGCAGCTCGA CGAGGCCTGG | 540 |
| GCCGGCGAGA ACTGCGGTCT GCTCGTGCGC GGTCTGAAGC GCGACGACGT CGAGCGCGGC | 600 |
| CAGGTGCTGG TGGAGCCGGG CTCCATCACC CCGCACACCA ACTTCGAGGC GAACGTCTAC | 660 |
| ATCCTGTCCA AGGACGAGGG TGGGCGTCAC ACCCCGTTCT ACTCGAACTA CCGCGCGCAG | 720 |
| TTCTACTTCC GCACCACCGA CGTCACCGGC GTCATCACGC TGCCCCGAGG CACCGAGATG | 780 |
| GTCATGCCCC GCGACACCAC CGAGATGTCG GTCGAGCTCA TCCAGCCGAT CGCCATGGAG | 840 |
| GAGGGCCTCG GCTTCGCCAT CCGCGAGGGT GGCCGCACCG TGGGCTCCGG C | 891 |

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(2) INFORMATION FOR SEQ ID NO: 160:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Mycobacterium tuberculosis*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

```

AACATGATCA CCGGCGCCGC GCAGATGGAC GGTGCGATCC TGGTGGTCGC CGCCACCGAC      60
GGCCCCGATGC CCCAGACCCG CGAGCACGTT CTGCTGGCGC GTCAAGTGGG TGTGCCCTAC      120
ATCCTGGTAG CGCTGAACAA GGCCGACGCA GTGGACGACG AGGAGCTGCT CGAACTCGTC      180
GAGATGGAGG TCCGCGAGCT GCTGGCTGCC CAGGAATTCG ACGAGGACGC CCCGTTGTG      240
CGGGTCTCGG CGCTCAAGGC GCTCGAGGGT GACGCGAAGT GGGTTGCCTC TGTCGAGGAA      300
CTGATGAACG CGGTGACGA GTCGATTCCG GACCCGGTCC GCGAGACCGA CAAGCCGTTT      360
CTGATGCCGG TCGAGGACGT CTTACCATTT ACCGGCCGCG GAACCGTGGT CACCGGACGT      420
GTGGAGCGCG GCGTGATCAA CGTGAACGAG GAAGTTGAGA TCGTCGGCAT TCGCCCATCG      480
ACCACCAAGA CCACCGTCAC CCGTGTGGAG ATGTTCCGCA AGCTGCTCGA CCAGGGCCAG      540
GCGGGCGACA ACGTTGGTTT GCTGCTGCGG GCGGTCAAGC GCGAGGACGT CGAGCGTGGC      600
CAGGTTGTCA CCAAGCCCGG CACCACCACG CCGCACACCG AGTTCGAAGG CCAGGTCTAC      660
ATCCTGTCCA AGGACGAGGG CGGCCGGCAC ACGCCGTTCT TCAACAATA CCGTCCGCAG      720
TTCTACTTCC GCACCACCGA CGTGACCGGT GTGGTGACAC TGCCGGAGGG CACCGAGATG      780
GTGATGCCCC GTGACAACAC CAACATCTCG GTGAAGTTGA TCCAGCCCGT CGCCATGGAC      840
GAAGGTCTGC GTTTCGCGAT CCGCGAGGGT GGCCGCACCG TGGGCGCCGG C              891

```

(2) INFORMATION FOR SEQ ID NO: 161:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: *Mycoplasma genitalium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

```

AATATGATCA CAGGTGCTGC ACAAATGGAT GGAGCTATTC TAGTTGTTTC AGCAACTGAT      60
AGTGTGATGC CCCAAACCCG CGAGCACATC TTAGTTGCCG GCCAAGTAGG GGTTCCTAAA      120
ATGGTAGTTT TTCTAAACAA GTGTGATATT GCTAGTGATG AAGAGGTACA AGAACTTGTT      180
GCTGAAGAAG TACGTGATCT GTTAACTTCC TATGGTTTTG ATGGTAAGAA CACTCCTATT      240
ATTTATGGCT CAGCTTTAAA AGCATTGGAA GGTGATCCAA AGTGGGAGGC TAAGATCCAT      300
GATTTGATTA AAGCAGTTGA TGAATGGATT CCAACTCCTA CACGTGAAGT AGATAAACCT      360
TTCTTATTAG CAATTGAAGA TACGATGACC ATTACTGGTA GAGGTACAGT TGTTACAGGA      420
AGAGTTGAAA GAGGTGAACT CAAAGTAGGT CAAGAAGTTG AAATTGTTGG TTTAAAACCA      480
ATTAGAAAAG CAGTTGTTAC TGAATTGAA ATGTTCAAAA AGGAACTTGA TTCAGCAATG      540
GCTGGTGACA ATGCTGGGGT ATTATTACGT GGTGTTGAAC GTAAAGAAGT TGAAAGAGGT      600
CAAGTTTTAG CAAAACCAGG CTCTATTAAA CCGCACAAGA AATTTAAAGC TGAGATCTAT      660
GCTTTAAGA AAGAAGAAGG TGGTAGACAC ACTGGTTTTT TAAACGGTTA CCGTCCTCAA      720
TTCTATTTCC GTACCACTGA TGTAAGTGGT TCTATTGCTT TAGCTGAAAA TACTGAAATG      780
GTTCTACCTG GTGATAATGC TTCTATTACT GTTGAGTTAA TTGCTCCTAT CGCTTGTGAA      840
AAAGGTAGTA AGTTCTCAAT TCGTGAAGGT GGTAGAACTG TAGGGGCAGG C      891

```

(2) INFORMATION FOR SEQ ID NO: 162:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Neisseria gonorrhoeae*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

```

AACATGATTA CCGGCGCCGC ACAAATGGAC GGTGCAATCC TGGTATGTTT TGCTGCCGAC      60
GGCCCTATGC CGCAAACCCG CGAACACATC CTGCTGGCCC GTCAAGTAGG CGTACCTTAC      120
ATCATCGTGT TCATGAACAA ATGCGACATG GTCGACGATG CCGAGCTGTT CCAACTGGTT      180
GAAATGGAAA TCCGCGACCT GCTGTCCAGC TACGACTTCC CCGGCGACGA CTGCCCCGATC      240

```

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```

GTACAAGGTT CCGCACTGAA AGCCTTGGAA GCGATGCCG CTTACGAAGA AAAAATCTTC      300
GAACTGGCTA CCGCATTGGA CAGATACATC CCGACTCCCG AGCGTGCCGT GGACAAACCA      360
TTCCTGCTGC CTATCGAAGA CGTGTTCTCC ATTTCCGGCC GCGGTACCGT AGTCACCGGC      420
CGTGTAGAGC GAGGTATCAT CCACGTTGGT GACGAGATTG AAATCGTCGG TCTGAAAGAA      480
ACCCAAAAAA CCACCTGTAC CGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGTCAG      540
GCGGGCGACA ACGTAGGCGT ATTGCTGCGC GGTACCAAAC GTGAAGACGT AGAACGCGGT      600
CAGGTATTGG CCAAACGGGG TACTATCACT CCTCACACCA AGTTCAAAGC AGAAGTGTAC      660
GTATTGAGCA AAGAAGAGGG CGGCCCCCAT ACCCCGTTTT TCGCCAACTA CCGTCCCCAA      720
TTCTACTTCC GTACCACTGA CGTAACCGGC ACGATTACTT TGGAAAAAGG TGTGAAATG      780
GTAATGCCGG GTGAGAACGT AACCATTACT GTAGAACTGA TTGCGCCTAT CGCTATGGAA      840
GAAGGTCTGC GCTTTGCGAT TCGCGAAGGC GGCCGTACCG TGGGTGCCGG C              891

```

(2) INFORMATION FOR SEQ ID NO: 163:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Rickettsia prowazekii*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

```

AATATGATAA CTGGTGCCGC TCAGATGGAT GGTGCTATAT TAGTAGTTTC TGCTGCTGAT      60
GGTCCTATGC CTCAAACTAG AGAACATATA TTAGTGCAA AACAGGTAGG TGTACCTGCT      120
ATGGTAGTAT TTTTGAATAA AGTAGATATG GTAGATGATC CTGACCTATT AGAATTAGTT      180
GAGATGGAAG TAAGAGAATT ATTATCAAAA TATGGTTTCC CTGGTAATGA AATACCTATT      240
ATTAAAGGTT CTGCACTTCA AGCTTTAGAA GGAAAACCTG AAGGTGAAAA AGCTATTAAT      300
GAGTTAATGA ATGCAGTAGA TACGTATATA CCTCAGCCTA TAGAGCTACA AGATAAACCT      360
TTTTTAATGC CAATAGAGGA TGTATTTTCT ATTTCAGGCA GAGGTACCGT TGTAAGTGGT      420
AGAGTGGAGT CAGGCATAAT TAAGGTGGGT GAAGAAATTG AAATAGTAGG TCTAAAAAAT      480
ACGCAAAAAA CCACTTGTAC AGGTGTAGAA ATGTTAGAAA AATTACTTGA TGAAGGACAA      540
TCTGGAGATA ATGTCGGTAT ATTACTACGT GGTACAAAAA GAGAAGAAGT AGAAAGAGGA      600

```

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| | |
|---|-----|
| CAAGTACTTG CAAAACCTGG GAGCATAAAA CCGCATGATA AATTTGAAGC TGAAGTGTAT | 660 |
| GTGCTTAGTA AAGAGGAAGG TGGACGTCAT ACCCCATTTA CTAATGATTA TCGCCCACAG | 720 |
| TTCTATTTTA GAACAACAGA TGTACCAGGC ACAATAAAAT TGCCTTCTGA TAAGCAGATG | 780 |
| GTTATGCCTG GAGATAATGC TACTTTTTCA GTAGAATTAA TTAAGCCGAT TGCTATGCAA | 840 |
| GAAGGGTTAA AATTCTCTAT ACGTGAAGGT GGTAGAACAG TAGGAGCCGG T | 891 |

(2) INFORMATION FOR SEQ ID NO: 164:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Salmonella typhimurium*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

| | |
|--|-----|
| AACATGATCA CCGGTGCTGC TCAGATGGAC GGCGCGATCC TGGTTGTTGC TCGCACTGAC | 60 |
| GGCCCGATGC CGCAGACCCG TGAGCACATC CTGCTGGGTC GTCAGGTAGG CGTTCCGTAC | 120 |
| ATCATCGTGT TCCTGAACAA ATGCGACATG GTTGATGACG AAGAGCTGCT GGAACGGTT | 180 |
| GAGATGGAAG TTCGCGAACT GCTGTCTCAG TACGACTTCC CGGGCGACGA CACTCCGATC | 240 |
| GTTCTGTTGTT CTGCTCTGAA AGCGCTGGAA GGCGACGCAG AGTGGGAAGC GAAAATCATC | 300 |
| GAACTGGCTG GCTTCCTGGA TTCTTATATT CCGGAACCAG AGCGTGCGAT TGACAAGCCG | 360 |
| TTCTGCTGTC CGATCGAAGA CGTATTCTCC ATCTCCGGTC GTGGTACCGT TGTACCGGT | 420 |
| CGTGTAGAGC GCGGTATCAT CAAAGTGGGC GAAGAAGTTG AAATCGTTGG TATCAAAGAG | 480 |
| ACTCAGAAGT CTACCTGTAC TGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGCCGT | 540 |
| GCCGGTGAGA ACGTAGGTGT TCTGCTGCGT GGTATCAAAC GTGAAGAAAT CGAACGTGGT | 600 |
| CAGGTACTGG CTAAGCCGGG CACCATCAAG CCGCACACCA AGTTCGAATC TGAAGTGTAC | 660 |
| ATTCTGTCCA AAGATGAAGG CGGCCGTCAT ACTCCGTTCT TCAAAGGCTA CCGTCCGCAG | 720 |
| TTCTACTTCC GTACTACTGA CGTGACTGGT ACCATCGAAC TGCCGGAAGG CGTAGAGATG | 780 |
| GTAATGCCGG GCGACAACAT CAAAATGGTT GTTACCCTGA TCCACCCGAT CGCGATGGAC | 840 |
| GACGGTCTGC GTTTCGCAAT CCGTGAAGGC GGCCGTACCG TTGGCGCGGG C | 891 |

(2) INFORMATION FOR SEQ ID NO: 165:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 881 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Shewanella putida*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

```

ATGATCACTG GTGCTGCACA GATGGACGGC GCGATTCTGG TAGTCGCTTC AACAGACGGT      60
CCAATGCCAC AGACTCGTGA GCACATCCTG CTTTCTCGTC AGGTGGCGT ACCATTCATC      120
ATCGTATTCA TGAACAAATG TGACATGGTA GATGACGAAG AGCTGTTAGA GCTAGTTGAG      180
ATGGAAGTGC GTGAAGTGT ATCAGAATAC GATTTCCCAG GTGATGACTT ACCGGTAATC      240
CAAGGTTTCA CTCTGAAAGC GCTAGAAGGC GAGCCAGAGT GGGAAGCAAA AATCCTTGAA      300
TTAGCAGCGG CGCTGGATTC TTACATTCCA GAACCACAAC GTGACATCGA TAAGCCGTTC      360
CTACTGCCAA TCGAAGACGT ATTCTCAATT TCAGGCCGTG GTACAGTAGT AACAGGTCGT      420
GTTGAGCGTG GTATTGTACG CGTAGGCGAC GAAGTTGAAA TCGTTGGTGT ACGTGCGACA      480
ACTAAGACAA CGTGACTGG TGTAGAAATG TTCCGTAAAC TGCTTGACGA AGGTCGTGCA      540
GGTGAGAACT GTGGTATTTT GTTACGTGGT ACTAAGCGTG ATGACGTAGA ACGTGGTCAA      600
GTATTAGCGA AGCCAGGTTC AATCAACCCA CACACTACTT TTGAATCAGA AGTTTACGTA      660
CTGTCAAAAG AAGAAGGTGG TCGTCACACG CCATTCTTCA AAGGCTACCG TCCACAGTTC      720
TACTTCCGTA CAACTGACGT AACC GG TACT ATCGA ACTGC CAGAAGGCGT AGAGATGGTA      780
ATGCCAGGCG ATAACATCAA GATGGTAGTG ACACTGATTT GCCCAATCGC GATGGACGAA      840
GGTTTACGCT TCGCAATCCG TGAAGGCGGT CGTACAGTGG T                                881

```

(2) INFORMATION FOR SEQ ID NO: 166:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 897 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Stigmatella aurantiaca*

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

| | |
|--|-----|
| AACATGATCA CGGGCGCGGC GCAGATGGAC GGAGCGATTC TGGTGGTGTC CGCGGCCGAC | 60 |
| GGCCCGATGC CCCAGACGCG TGAGCACATC CTGCTGGCCA GGCAGGTGGG CGTGCCCTAC | 120 |
| ATCGTCGTCT TCCTGAACAA GGTGGACATG CTGGACGATC CGGAGCTGCG CGAGCTGGTG | 180 |
| GAGATGGAGG TGC GCGACCT GCTCAAGAAG TACGAGTTCC CGGGCGACAG CATCCCCATC | 240 |
| ATCCCTGGCA GCGCGCTCAA GCGCTGGAG GGAGACACCA GCGACATCGG CGAGGGAGCG | 300 |
| ATCCTGAAGC TGATGGCGGC GGTGGACGAG TACATCCCGA CGCCGCAGCG TCGACGGAC | 360 |
| AAGCCGTTCC TGATGCCGGT GGAAGACGTG TTCTCCATCG CAGGCCGAGG AACGGTGGCG | 420 |
| ACGGGCCGAG TGGAGCGCG CAAGATCAAG GTGGCGAGG AAGTGGAGAT CGTGGGGATC | 480 |
| CGTCCGACGC AGAAGACGGT CATCACGGGG GTGGAGATGT TCCGCAAGCT GCTGGACGAG | 540 |
| GGCATGGCGG GAGACAACAT CGGAGCGCTG CTGCGAGGCC TGAAGCGCGA GGACCTGGAG | 600 |
| CGTGGGCAGG TGCTGGCGAA CTGGGGGAGC ATCAACCCGC ACACGAAGTT CAAGGCGCAG | 660 |
| GTGTACGTGC TGTCGAAGGA AGAGGGAGGG CGGCACACGC CGTTCTTCAA GGGATACCGG | 720 |
| CCGCAGTTCT ACTTCCGGAC GACGGACGTG ACCGGAACGG TGAAGCTGCC GGACAACGTG | 780 |
| GAGATGGTGA TGCCGGGAGA CAACATCGCC ATCGAGGTGG AGCTCATTAC TCCGGTCGCC | 840 |
| ATGGAGAAGG AGCTGCCGTT CGCCATCCGT GAGGGTGGCC GCACGGTGGG CGCCGGC | 897 |

(2) INFORMATION FOR SEQ ID NO: 167:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Streptococcus pyogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

| | |
|---|-----|
| AACATGATCA CTGGTGCCGC TCAAATGGAC GGAGCTATCC TTGTAGTTGC TTCAACTGAT | 60 |
| GGACCAATGC CACAACTCG TGAGCACATC CTTCTTTCAC GTCAGGTGG TGTAAACAC | 120 |
| CTTATCGTGT TCATGAACAA AGTTGACCTT GTTGATGACG AAGAGTTGCT TGAATTAGTT | 180 |
| GAGATGGAAA TTCGTGACCT TCTTTCAGAA TACGATTTC CAGGTGATGA CCTTCCAGTT | 240 |
| ATCCAAGGTT CAGCTCTTAA AGCTCTTGAA GCGGACACTA AATTGAAGA CATCATCATG | 300 |

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| | |
|---|-----|
| GAATTGATGG ATACTGTTGA TTCATACATT CCAGAACCAG AACGCGACAC TGACAAACCA | 360 |
| TTGCTTCTTC CAGTCGAAGA CGTATTCTCA ATTACAGGTC GTGGTACAGT TGCTTCAGGA | 420 |
| CGTATCGACC GTGGTACTGT TCGTGTCAAC GACGAAATCG AAATCGTTGG TATCAAAGAA | 480 |
| GAAACTAAAA AAGCTGTTGT TACTGGTGTT GAAATGTTCC GTAAACAAC TACGAAGGT | 540 |
| CTTGCAGGAG ACAACGTAGG TATCCTTCTT CGTGGTGTTT AACGTGACGA AATCGAACGT | 600 |
| GGTCAAGTTA TTGCTAAACC AAGTTCAATC AACCCACACA CTAAATTCAA AGGTGAAGTA | 660 |
| TATATCCTTT CTAAAGACGA AGGTGGACGT CACACTCCAT TCTTCAACAA CTACCGTCCA | 720 |
| CAATTCTACT TCCGTACAAC TGACGTAACA GGTTCATCG AACTTCCAGC AGGTACAGAA | 780 |
| ATGGTTATGC CTGGTGATAA CGTGACAATC AACGTTGAGT TGATCCACCC AATCGCCGTA | 840 |
| GAACAAGGTA CTACTTTCTC AATCCGTGAA GGTGGACGTA CTGTTGGTTC AGGT | 894 |

(2) INFORMATION FOR SEQ ID NO: 168:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 897 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Thiobacillus cuprinus*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

| | |
|--|-----|
| AACATGATCA CCGGTGCGGC CCAGATGGAC GGCGCCATCC TGGTCGTGTC CGCCGCCGAC | 60 |
| GGCCCCATGC CCCAAACCCG CGAGCACATC CTGCTGGCGC GTCAGGTGGG CGTGCCCTAC | 120 |
| ATCATCGTGT TCCTCAACAA GTGCGACATG GTCGACGACG CCGAGCTGCT CGAACTCGTC | 180 |
| GAGATGGAAG TGC GCGAGCT GCTGTCCAAG TACGACTTCC CCGGTGACGA CACCCCCATC | 240 |
| ATCAAGGGCT CGGCCAAGCT GGCCCTCGAA GGC GACAAGG GCGAACTGGG CGAAGGCGCC | 300 |
| ATTCTCAAGC TG GCGAGGC CCTGGACACC TACATCCCCA CGCCCGAGCG GGCCGTGAC | 360 |
| GGCGCGTTCC TCATGCCCGT GGAAGACGTG TTCTCCATCT CCGGGCGCGG CACGGTGGTC | 420 |
| ACCGGGCGTG TGGAGCGCG CATCATCAAG GTCGGCGAGG AAATCGAGAT TGTCGGCCTC | 480 |
| AAGCCCACCC TCAAGACCAC CTGCACCGGC GTGGAAATGT TCAGGAAGCT GCTCGACCAG | 540 |
| GGCCAGGCCG GCGACAACGT CGGCATCTTG CTGCGCGGCA CCAAGCGCGA GGAAGTCGAG | 600 |
| CGCGGCCAGG TGCTGTGCAA ACCCGGCTCG ATCAAGCCCC ACACCCACTT CACCGCCGAG | 660 |

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| | |
|---|-----|
| GTGTACGTGC TGAGCAAGGA CGAGGGCGGC CGCCACACCC CCTTCTTCAA CAACTACCGC | 720 |
| CCGCAGTTCT ACTTCCGCAC CACCGACGTC ACCGGCGCCA TCGAACTGCC CAAGGACAAG | 780 |
| GAAATGGTCA TGCCCGGCGA TAATGTGAGC ATCACCGTCA AGCTCATCGC CCCCATCGCC | 840 |
| ATGGAAGAAG GCCTGCGCTT CGCCATCCGC GAAGGCGGCC GCACCGTCGG CGCCGGC | 897 |

(2) INFORMATION FOR SEQ ID NO: 169:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 894 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Treponema pallidum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

| | |
|---|-----|
| AATATGATCA CGGGTGCTGC GCAGATGGAC GGTGGTATTC TCGTCGTGTC TGCGCCTGAC | 60 |
| GGCGTTATGC CACAGACGAA GGAGCATCTT CTGCTCGCCC GTCAGGTGG TGTCCCTCC | 120 |
| ATCATTGTTT TTTTGAACAA GGTGATTG GTTGATGATC CTGAGTTGCT AGAGCTGGTG | 180 |
| GAAGAAGAGG TCGTGATGC GCTTGCTGGA TATGGGTTTT CGCGTGAGAC GCCTATCGTC | 240 |
| AAGGGTCTG CGTTTAAAGC TCTGCAGGAT GGCGCTTCCC CGGAGGATGC AGCTTGATT | 300 |
| GAGGAACTGC TTGCGGCCAT GGATTCCTAC TTTGAAGACC CAGTGCGTGA CGACGCAAGA | 360 |
| CCTTCTTGC TCTCTATCGA GGATGTGTAC ACTATTTCTG GGCGTGGTAC CGTTGTCACG | 420 |
| GGGCGCATCG AATGTGGGGT AATTAGTCTG AATGAAGAGG TCGAGATCGT CGGGATTAAG | 480 |
| CCCACTAAGA AAACAGTGGT TACTGGCATT GAGATGTTA ATAAGTTGCT TGATCAGGGA | 540 |
| ATTGCAGGTG ATAACGTGGG GCTGCTTTTG CGCGGGGTGG ATAAAAAGA GGTGAGCGC | 600 |
| GGTCAGGTGC TTTCTAAGCC CGGTTCTATT AAGCCACACA CCAAGTTTGA GGCGCAGATC | 660 |
| TACGTGCTCT CTAAGGAAGA GGGTGGCCGT CACAGTCCTT TTTTCAAGG TTATCGTCCG | 720 |
| CAGTTTATT TTAGAACTAC TGACATTACC GGTACGATTT CTCTTCCTGA AGGGGTAGAC | 780 |
| ATGGTGAAGC CGGGGGATAA CACCAAGATT ATAGGTGAGC TCATCCACCC GATAGCTATG | 840 |
| GACAAGGGTC TGAAGCTTGC GATTCGTGAA GGGGGGCGCA CTATTGCTTC TGGT | 894 |

(2) INFORMATION FOR SEQ ID NO: 170:

(i) SEQUENCE CHARACTERISTICS:

- 153 -

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Ureaplasma urealyticum*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

```

AATATGATTA CAGGGGCAGC ACAAATGGAT GGAGCAATTT TAGTTATTGC TGCATCTGAT      60
GGGGTTATGG CTCAAACTAA AGAACATATT TTATTAGCAC GTCAAGTTGG TGTTCACAAA      120
ATCGTTGTTT TCTTAAACAA ATGTGATTTT ATGACAGATC CAGATATGCA AGATCTTGTT      180
GAAATGGAAG TTCGTGAATT ATTATCTAAA TATGGATTTG ATGGCGATAA CACACCAGTT      240
ATTCGTGGTT CAGGTCTTAA GGCTTTAGAA GGAGATCCAG TTTGAGAAGC AAAAATTGAT      300
GAATTAATGG ACGCAGTTGA TTCATGAATT CCATTACCAG AACGTAGTAC TGACAAACCA      360
TTCTTATTAG CAATTGAAGA TGTATTCACA ATTCAGGAC GTGGTACAGT AGTAACTGGA      420
CGTGTGAAC  GTGGTGTATT AAAAGTTAAT GATGAGGTTG AAATTGTTGG TCTAAAAGAC      480
ACTCAAAAAA CTGTTGTGTTAC AGGAATTGAA ATGTTTAGAA AATCATTAGA TCAAGCTGAA      540
GCTGGTGATA ATGCTGGTAT TTTATTACGT GGTATTAAAA AAGAAGATGT TGAACGTGGT      600
CAAGTACTTG TAAAACCAGG ATCAATTAAA CCTCACCGTA CTTTTACTGC TAAAGTTTAT      660
ATTCTTAAAA AAGAAGAAGG TGGACGTCAT ACACCTATTG TTTCAGGATA CCGTCCACAA      720
TTCTATTTTA GAACAACAGA TGTAACAGGT GCTATTTTAT TACCTGCTGG TGTTGATTG      780
GTTATGCCAG GTGATGACGT TGAAATGACT GTAGAATTAA TTGCTCCAGT TGCGATTGAA      840
GATGGATCTA AATTCTCAAT CCGTGAAGGT GGTAAACTG  TAGGTCATGG T      891

```

(2) INFORMATION FOR SEQ ID NO: 171:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 909 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Wolinella succinogenes*

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

- 154 -

| | |
|---|-----|
| AACATGATTA CAGGTGCTGC TCAAATGGAT GGC GCGATTC TTGTTGTTTC TCGGCGGAT | 60 |
| GGCCCCATGC CCCAACTAG GGAGCACATT CTTCTTTCTC GACAAGTAGG CGTTCCTTAC | 120 |
| ATCGTGGTTT TCTTGAACAA AGAAGATATG GTTGATGACG CTGAGCTTCT TGAGCTTGTT | 180 |
| GAAATGGAAG TTAGAGAACT TCTTAGCAAC TACGACTTCC CTGGAGATGA CACTCCTATC | 240 |
| GTTGCAGGTT CCGCTCTTAA AGCTCTTGAA GAGGCTAACG ACCAGGAAAA TGTTGGCGAG | 300 |
| TGGGGCGAGA AAGTATTGAA GCTTATGGCT GAGGTTGACC GATATATTCC TACGCCTGAG | 360 |
| CGAGATGTGG ATAAGCCTTT CTTATGCCT GTTGAAGACG TATTCTCCAT CGCGGGTCGT | 420 |
| GGAACCGTTG TGACAGGAAG AATTGAAAGA GCGTGGTTA AAGTCGGTGA CGAAGTAGAA | 480 |
| ATCGTTGGTA TCCGAAACAC ACAAAAAACA ACCGTAACG GCGTTGAGAT GTTCCGAAAA | 540 |
| GAGCTCGACA AGGGTGAGGC GGGTGACAAC GTTGGTGTTT TTTTGAGAGG CACCAAGAAA | 600 |
| GAAGATGTTG AGAGAGGTAT GGTTCTTTGT AAAATAGGTT CTATCACTCC TCACACTAAC | 660 |
| TTTGAAGGTG AAGTTTACGT TCTTTCCAAA GAGGAAGGCG GACGACACAC TCCATTCTTC | 720 |
| AATGGATACC GACCTCAGTT CTATGTTAGA ACTACAGACG TTACCGGTTT TATCTCTCTT | 780 |
| CCTGAGGGCG TAGAGATGGT TATGCCTGGT GACAACGTTA AGATCAATGT TGAGCTTATC | 840 |
| GCTCCTGTAG CCCTCGAAGA GGGAACACGA TTCGCGATCC GTGAAGGTGG TCGAACCGTT | 900 |
| GGTGCGGGT | 909 |

(2) INFORMATION FOR SEQ ID NO: 172:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /note= "n = inosine"

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "n = inosine"

- 155 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

TARTCNGTRA ANGCYTCNAC RCACAT

26

(2) INFORMATION FOR SEQ ID NO: 173:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

TCTTTAGCAG AACAGGATGA A

21

(2) INFORMATION FOR SEQ ID NO: 174:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

GAATAATTCC ATATCCTCCG

20

CLAIMS**What is claimed is:**

1. A method using probes and/or amplification primers which are specific, ubiquitous and sensitive for determining the presence and/or amount of nucleic acids:
 - 5 - from a bacterial antibiotic resistance gene selected from the group consisting of *bla_{tem}*, *bla_{shv}*, *bla_{rob}*, *bla_{oxa}*, *bla_Z*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aac6'-IIa*, *aacA4*, *aad(6')*, *vanA*, *vanB*, *vanC*, *msrA*, *satA*, *aac(6'')-aph(2'')*, *vat*, *vga*, *ermA*, *ermB*, *ermC*, *mecA*, *int* and *sul*, and
 - from specific bacterial and fungal species selected from the group consisting
 - 10 of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species,
- in any sample suspected of containing said bacterial and/or fungal nucleic acids,
- 15 wherein each of said nucleic acid or variant or part thereof comprises a selected target region hybridizable with said probes or primers;
 - said method comprising the following steps: contacting said sample with said probes or primers and detecting the presence and/or amount of hybridized probes or amplified products as an indication of the presence and/or amount of said specific
 - 20 bacterial and/or fungal species and bacterial antibiotic resistance genes.
2. A method according to claim 1, which further makes use of probes and/or primers which are specific, ubiquitous and sensitive for determining the presence and/or amount of nucleic acids from any bacterium or fungus.
3. The method of claim 1, which is performed directly from a test sample.
- 25 4. The method of claim 1, which is performed directly from a test sample consisting of a bacterial and/or fungal culture or suspension.
5. The method of claim 1, wherein said nucleic acids are all detected under uniform hybridization or amplification conditions.
6. The method of claim 1, wherein said nucleic acids are amplified by a method
 - 30 selected from the group consisting of:
 - a) polymerase chain reaction (PCR),
 - b) ligase chain reaction (LCR),
 - c) nucleic acid sequence-based amplification (NASBA),

- d) self-sustained sequence replication (3SR),
- e) strand displacement amplification (SDA),
- f) branched DNA signal amplification (bDNA),
- g) transcription-mediated amplification (TMA),
- 5 h) cycling probe technology (CPT),
- i) nested PCR, and
- j) multiplex PCR.

7. The method of claim 6, wherein said nucleic acids are amplified by PCR.

8. The method of claim 7, wherein the PCR protocol achieves within one hour
10 under uniform amplification conditions the determination of the presence of said nucleic acids by performing for each amplification cycle an annealing step of thirty seconds at 45-55°C and a denaturation step of only one second at 95°C without any time specifically allowed to an elongation step.

9. A method for the detection, identification and/or quantification of a
15 microorganism selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, directly from a test sample or from bacterial and/or fungal cultures, which comprises the following
20 steps:

a) depositing and fixing on an inert support or leaving in solution the said microorganism DNA of the sample or of a substantially homogeneous population of said microorganism isolated from this sample, or

inoculating said sample or said substantially homogeneous population of
25 microorganism isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or said isolated microorganism to release the said microorganism DNA,

said microorganism DNA being made in a substantially single-stranded form;

b) contacting said single-stranded DNA with a probe, said probe comprising at
30 least one single-stranded nucleic acid which nucleotide sequence is selected from the group consisting of SEQ ID NOs: 26, 27, 28, 29, 30, 120, 131 to 134, 31, 140 to 143, 32 to 36, 120 to 124, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of *Enterococcus faecium*, *Listeria*

monocytogenes, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, respectively, under conditions such that the nucleic acid of said probe can selectively hybridize with
5 said microorganism DNA, whereby a hybridization complex is formed; and

c) detecting the presence of said hybridization complex on said inert support or in said solution as an indication of the presence and/or amount of said microorganism, in said test sample.

10. A method for detecting the presence and/or amount of a microorganism
10 selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, in a test sample which comprises the following steps:

15 a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said microorganism DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an
20 extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 26, 27, 28, 29, 30, 120, 131 to 134, 31, 140 to 143, 32 to 36, 120 to 124, respectively with regard to said microorganism, a sequence complementary thereof, and a variant thereof;

25 b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of said microorganisms, in said test
30 sample.

11. The method of claim 10, wherein said pair of primers is defined in SEQ ID NOs: 1 and 2, 3 and 4, 5 and 6, 7 and 8, 9 and 10, 11 and 12, 13 and 14, 15 and 16, 17 to 20, 21 and 22, respectively, for each of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species and *Streptococcus* species.
35

12. A method for detecting the presence and/or amount of any bacterium directly from a test sample or a bacterial culture, which comprises the following steps:

5 a) depositing and fixing on an inert support or leaving in solution the bacterial DNA of the sample or of a substantially homogeneous population of bacteria isolated from this sample, or

inoculating said sample or said substantially homogeneous population of bacteria isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated bacteria to release the bacterial DNA,

said bacterial DNA being made in a substantially single-stranded form;

10 b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleic acid which nucleotide sequence is selected from the group consisting of SEQ ID NOs: 118, 119, 125 to 171, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of any
15 bacterial species, under conditions such that the nucleic acid of said probe can selectively hybridize with said bacterial DNA, whereby a hybridization complex is formed; and

c) detecting the presence of said hybridization complex on said inert support or in said solution as an indication of the presence and/or amount of any bacterium in
20 said test sample.

13. A method for detecting the presence and/or amount of any bacterium in a test sample which comprises the following steps:

a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers
25 being capable of hybridizing selectively with one of the two complementary strands of any bacterial DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NO:
30 118, 119, 125 to 171, a sequence complementary thereof, and a variant thereof;

b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

c) detecting the presence and/or amount of said amplified target sequence as
35 an indication of the presence and/or amount of any bacterium in said test sample.

14. The method of claim 13, wherein said pair of primers is defined in SEQ ID NOs: 23 and 24.

15. A method for obtaining *tuf* sequences from any bacterium directly from a test sample or a bacterial culture, which comprises the following steps:

5 a) treating said sample with an aqueous solution containing a pair of primers having a sequence selected within the nucleotide sequences defined in SEQ ID NOs: 107 and 108, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, and a variant thereof, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said bacterial *tuf*
10 gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;

b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any,
15 to a detectable level; and

c) detecting the presence and/or amount of said amplified target sequence; and

d) determining the nucleotide sequence of the said amplified target sequence by using any DNA sequencing method.

16. A method for detecting the presence and/or amount of any fungus directly from
20 a test sample or a fungal culture, which comprises the following steps:

a) depositing and fixing on an inert support or leaving in solution the fungal DNA of the sample or of a substantially homogeneous population of fungi isolated from this sample, or

inoculating said sample or said substantially homogeneous population of fungi
25 isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated fungi to release the fungal DNA,

said fungal DNA being made in a substantially single-stranded form;

b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleotide sequence selected from the group consisting of
30 SEQ ID NOs: 120 to 124, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of any fungus, under conditions such that the nucleic acid of said probe can selectively hybridize with said fungal DNA, whereby a hybridization complex is formed; and

35 c) detecting the presence of said hybridization complex on said inert support or

in said solution as an indication of the presence and/or amount of any fungus in said test sample.

17. A method for detecting the presence and/or amount of any fungus in a test sample which comprises the following steps:

- 5 a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of any fungal DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product
10 which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 120 to 124, a sequence complementary thereof, and a variant thereof;

- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any,
15 to a detectable level; and

 c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of any fungus in said test sample.

18. A method for obtaining *tuf* sequences from any fungus directly from a test sample or a fungal culture, which comprises the following steps:

- 20 a) treating said sample with an aqueous solution containing a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 109 and 172, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, and a variant thereof, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said fungal *tuf*
25 gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;

- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any,
30 to a detectable level; and

 c) detecting the presence and/or amount of said amplified target sequence; and

 d) determining the nucleotide sequence of the said amplified target sequence by using any DNA sequencing method.

19. A method as defined in claim 1, which comprises the evaluation of the presence
35 of a bacterial resistance mediated by a bacterial antibiotic resistance gene selected

from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, directly from a test sample or a bacterial culture, which comprises the following steps:

5 a) depositing and fixing on an inert support or leaving in solution the bacterial DNA of the sample or of a substantially homogeneous population of bacteria isolated from this sample, or

inoculating said sample or said substantially homogeneous population of bacteria isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated bacteria to release the bacterial DNA,

said bacterial DNA being made in a substantially single-stranded form;

10 b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleotide sequence having at least 12 nucleotide in length is selected from the group consisting of SEQ ID NOs: 110, 111, 112, 113, 114 115, 116, 117, a sequence complementary thereof, and a variant thereof, which specifically hybridizes with said bacterial antibiotic resistance gene, respectively; and

15 c) detecting the presence of a hybridization complex as an indication of a bacterial resistance mediated by said one of said bacterial antibiotic resistance genes.

20. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance mediated by a bacterial antibiotic resistance gene selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*,
20 directly from a test sample or a bacterial culture, which comprises the following steps:

a) treating said sample with an aqueous solution containing at least one pair of primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said bacterial antibiotic resistance gene that contains a target sequence, and the other of said
25 primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 110, 111, 112, 113, 114, 115, 116, 117, respectively with regard to said bacterial antibiotic resistance gene, a sequence complementary thereof, and a
30 variant thereof;

b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and

35 c) detecting the presence and/or amount of said amplified target sequence as an indication of a bacterial resistance mediated by one of said bacterial antibiotic resistance genes.

21. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance gene selected from the group consisting of *bla_{tem}*, *bla_{shv}*, *bla_{rob}*, *bla_{oxa}*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aac6'-IIa*, *aacA4*, *aad(6')*, *vanA*, *vanB*, *vanC*, *msrA*, *satA*, *aac(6')-aph(2'')*, *vat*, *vga*, *ermA*, *ermB*, *ermC*, *mecA*, *int* and *sul*, directly
5 from a test sample or a bacterial culture, which comprises the following steps:

a) treating said sample with an aqueous solution containing at least one pair of primers having a sequence selected in the group consisting of SEQ ID NOs: 37 to 40, 41 to 44, 45 to 48, 49 and 50, 51 and 52, 53 and 54, 55 and 56, 57 and 58, 59 to 60, 61 to 64, 65 and 66, 173 and 174, 67 to 70, 71 to 74, 75 and 76, 77 to 80, 81 and 82,
10 83 to 86, 87 and 88, 89 and 90, 91 and 92, 93 and 94, 95 and 96, 97 and 98, 99 to 102, 103 to 106, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, a variant thereof, and mixtures thereof, one of said primers of said pair being capable of hybridizing selectively with one of the two complementary strands of its respective bacterial antibiotic resistance gene that contains a target
15 sequence, and the other of said primers of said pairs being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;

b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any,
20 to a detectable level; and

c) detecting the presence and/or amount of said amplified target sequence as an indication of a bacterial resistance mediated by one of said bacterial antibiotic resistance genes.

22. A nucleic acid having the nucleotide sequence of any one of SEQ ID NOs: 26 to 36, 110 to 171, a part thereof, a sequence complementary thereof, and variant thereof which, when in single-stranded form, ubiquitously and specifically hybridizes with a target bacterial or fungal DNA as a probe or as a primer.

23. An oligonucleotide having the nucleotide sequence of any one of SEQ ID NOs: 1 to 25, 37 to 109, 172 to 174, a part thereof, a sequence complementary thereof, and
30 variant thereof, which ubiquitously and specifically hybridizes with a target bacterial or fungal DNA as a probe or as a primer.

24. A recombinant plasmid comprising a nucleic acid as defined in claim 22.

25. A recombinant host which has been transformed by a recombinant plasmid according to claim 24.

35 26. A recombinant host according to claim 25 wherein said host is *Escherichia coli*.

27. A diagnostic kit for the detection and/or quantification of the nucleic acids of any

- combination of the microbial species and/or genera selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, comprising any suitable combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 26 to 36, 120 to 124, 131 to 134, 140 to 143, sequences complementary thereof, and variants thereof.
28. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the microbial species and/or genera selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 26 to 36, 120 to 124, 131 to 134, 140 to 143, sequences complementary thereof, and variants thereof.
29. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the microbial species and/or genera selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species and *Streptococcus* species, comprising any suitable combination of primers selected from the group consisting of SEQ ID NOs: 1 to 22, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.
30. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, comprising any suitable combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof.
31. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof.

32. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of *bla_{temp}*, *bla_{shv}*, *bla_{rob}*, *bla_{oxa}*, *bla_Z*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aac6'-IIa*, *aacA4*, *aad(6')*, *vanA*, *vanB*, *vanC*, *msrA*, *satA*, *aac(6')-aph(2'')*, *vat*, *vga*, *ermA*, *ermB*, *ermC*, *mecA*, *int* and *sul*, comprising any suitable combination of primers selected from the group consisting of SEQ ID NOs: 37 to 106, 173 and 174, a part thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.

A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium and/or fungus, comprising any combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof.

34. A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium and/or fungus, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof.

35. A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium, comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.

36. A diagnostic kit, as defined in claim 27, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

37. A diagnostic kit, as defined in claim 28, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

38. A diagnostic kit, as defined in claim 29, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.

39. A diagnostic kit, as defined in claim 27, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from

the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*.

- 5 40. A diagnostic kit, as defined in claim 28, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-IIa*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*.

- 10 41. A diagnostic kit, as defined in claim 29, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 37 to 106, 173 and 174, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla_{tem}*, *bla_{rob}*, *bla_{shv}*, *bla_{oxa}*, *blaZ*, *aadB*, *aacC1*, *aacC2*, *aacC3*, *aacA4*, *aac6'-IIa*, *aad(6')*, *ermA*, *ermB*, *ermC*, *mecA*, *vanA*, *vanB*, *vanC*, *safA*, *aac(6')-aph(2'')*, *vat*, *vga*, *msrA*, *sul* and *int*.

- 15 42. A diagnostic kit, as defined in claim 30, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

- 20 43. A diagnostic kit, as defined in claim 31, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

- 25 44. A diagnostic kit, as defined in claim 32, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.

- 30 45. A diagnostic kit, as defined in claim 39, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

acids of any bacterium and/or fungus.

46. A diagnostic kit, as defined in claim 40, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences
5 complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.

47. A diagnostic kit, as defined in claim 41, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences
10 complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 97/00829

| A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12Q1/68 | | |
|---|--|--|
| According to International Patent Classification (IPC) or to both national classification and IPC | | |
| B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12Q | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched | | |
| Electronic data base consulted during the international search (name of data base and, where practical, search terms used) | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | WO 96 08582 A (BERGERON MICHEL G ;OUELLETTE MARC (CA); ROY PAUL H (CA)) 21 March 1996 see whole document, esp claims 1-3 --- | 1-14, 19-38, 40-47 |
| X | FR 2 699 539 A (PASTEUR INSTITUT) 24 June 1994 see whole document, esp. abstract and claims --- -/-- | 1-8,19, 32 |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex. | | |
| * Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "A" document member of the same patent family | | |
| Date of the actual completion of the international search 8 June 1998 | | Date of mailing of the international search report 01.07.98 |
| Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | | Authorized officer Müller, F |

INTERNATIONAL SEARCH REPORT

Intern. Appl. Application No
PCT/CA 97/00829

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 97/00829

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A,P | <p>EP 0 761 815 A (SANDOZ AG ;SANDOZ LTD (CH); SANDOZ AG (DE)) 12 March 1997 see the whole document & DATABASE GENESEQ DERWENT AC:T87876</p> | <p>1,21</p> |
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 97/00829

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
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| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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INTERNATIONAL SEARCH REPORT

Inter. Appl. Application No
PCT/CA 97/00829

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 97/00829

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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| X | <p>DATABASE EMPRO EMBL LUDWIG W. ET AL.: "Phylogenetic relationships of bacteria based on comparative sequence analysis of elongation factor Tu and ATP-synthase-beta subunit genes; Antonie van leeuwenhoek 64; 285-305 (1993)" XP002067256 AC: X76863, X76866, X76867, X76871, X76872</p> | 22 |
| P,X | <p>EP 0 786 519 A (HUMAN GENOME SCIENCES INC) 30 July 1997 seq id 4</p> | 22 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 97/00829

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-13,19,21-29,32-34,36,41-43,45,46 (partly)

Nucleic acids (SEQ. ID.:1,2,13,14,67-70,51,52, 71-76, 81-86,131-134, 173,174) specific for Enterococcus spp., methods using them, and plasmids, hosts and kits containing them

2. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ ID.: 3,4, 136-139) specific for Listeria monocytogenes, methods using them, and plasmids, hosts and kits containing them

3. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ. ID.: 5,6,15,16,162) specific for Neisseria spp., methods using them, and plasmids, hosts and kits containing them

4. Claims: 1-9,11-13,21-26,32-34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ ID.: 7,8,17-20,77-80,89-98, 140-143) specific for Staphylococcus spp., methods using them, and plasmids, hosts and kits containing them

5. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ. ID.: 9,10,21,22,144-146,167) specific for Streptococcus spp., methods using them, and plasmids, hosts and kits containing them

6. Claims: 1-12,22-29,33,34,36,37,42,43,45,46 (partly), 16, 17 (complete)

Nucleic acids (SEQ ID.: 11,12,120-124) specific for Candida albicans, methods using them, and plasmids, hosts and kits containing them

7. Claims: 14,19,20,30,31,35,38,39,40,44,47 (complete), 23, 32 (partly)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Nucleic acids (SEQ ID.: 23-24, 99-106, 110-117, 118,119, 125-130, 135, 147-161, 163-166, 168-171) specific for universal detection of bacteria and fungus species, methods using them, and plasmids, hosts and kits containing them

8. Claims: 15,18 (complete)

Methods for obtaining tuf sequences by using SEQ ID.: 107,108,109 and 172

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 97/00829

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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